

PROTOCOL No. PM-8450

COVANCE STUDY No. 12226-8450

DRAFT 1

RESEARCH STUDY REPORT

24 JULY 2002

VOL 2 of 25

Pgs. 182 TO 860

PM3006438761

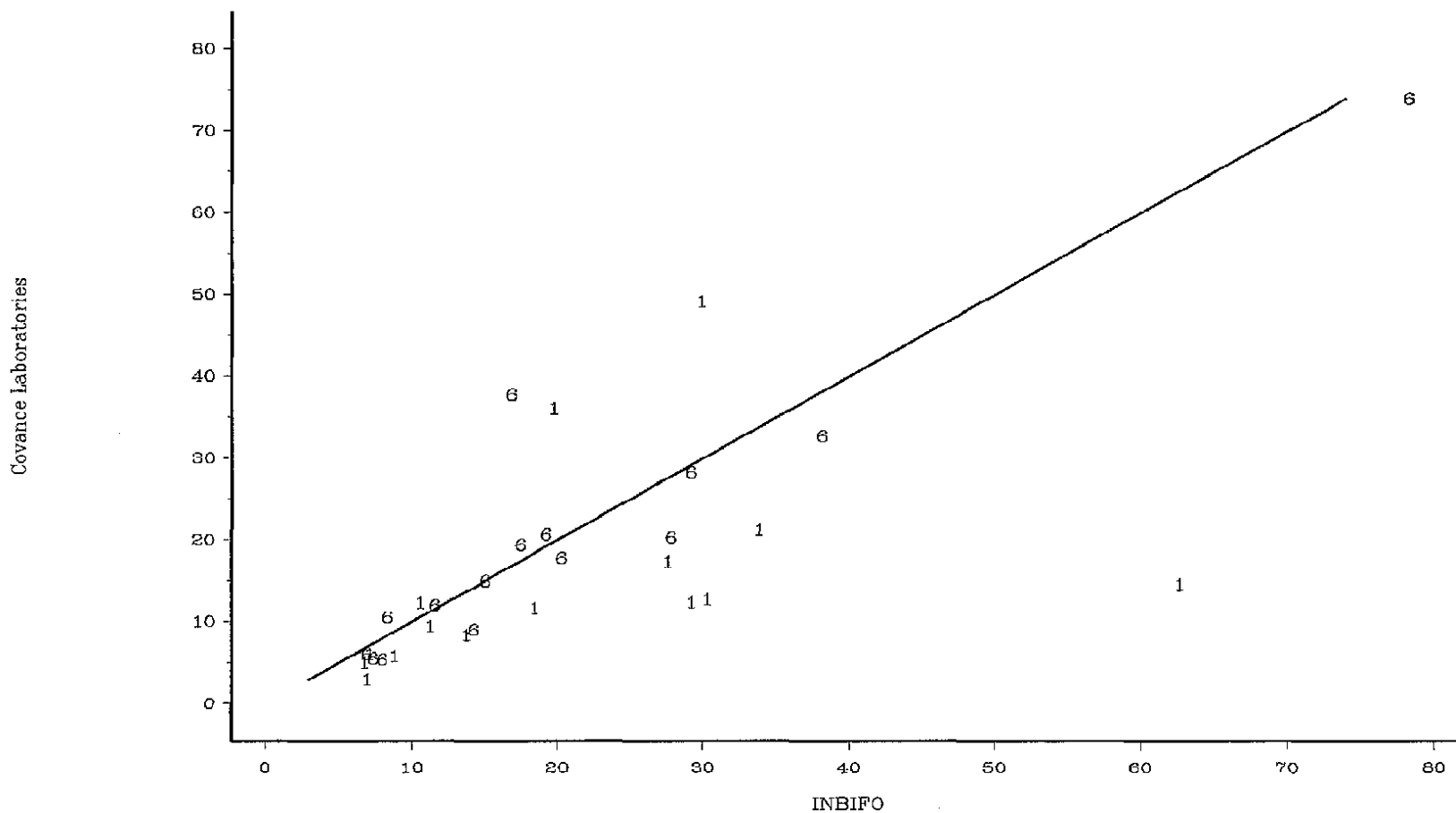
RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Plasma Blood Biomarker of Exposure:
4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 6=Week 6

Figure 14.1.4.1-1
Covance by INBIFO for 4-Aminobiphenyl-Hb Adduct (pg/g hemoglobin)

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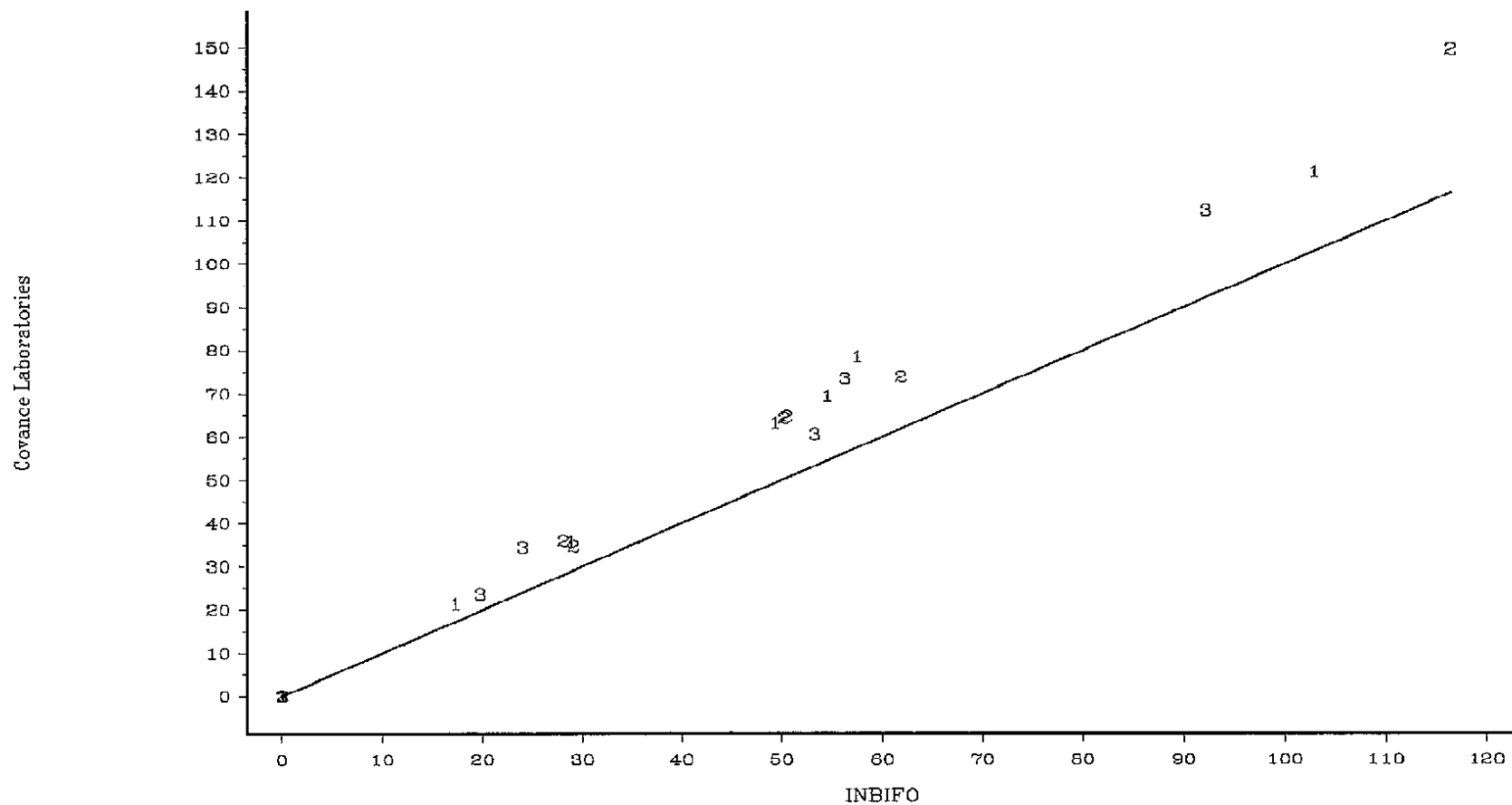
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Protocol No. PM-8450

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24-Hour Urine Biomarker of Exposure:
Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-2
Covance by INBIFO for Sum of Nicotine and Nicotine Metabolites (nmol/mg Creatinine)

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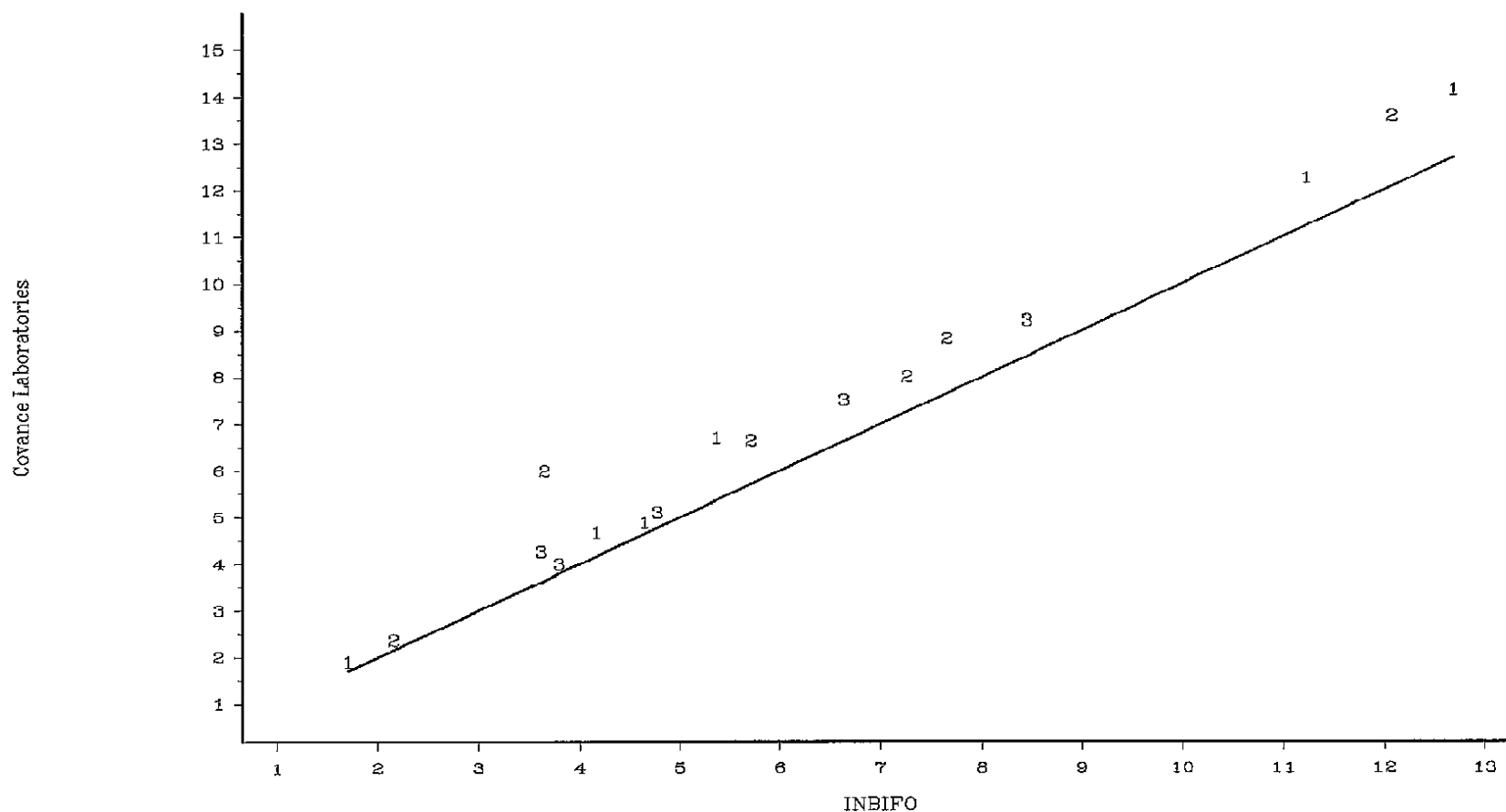
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24-Hour Urine Biomarker of Exposure:
Nicotine (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-3
Covance by INBIFO for Nicotine (nmol/mg Creatinine)

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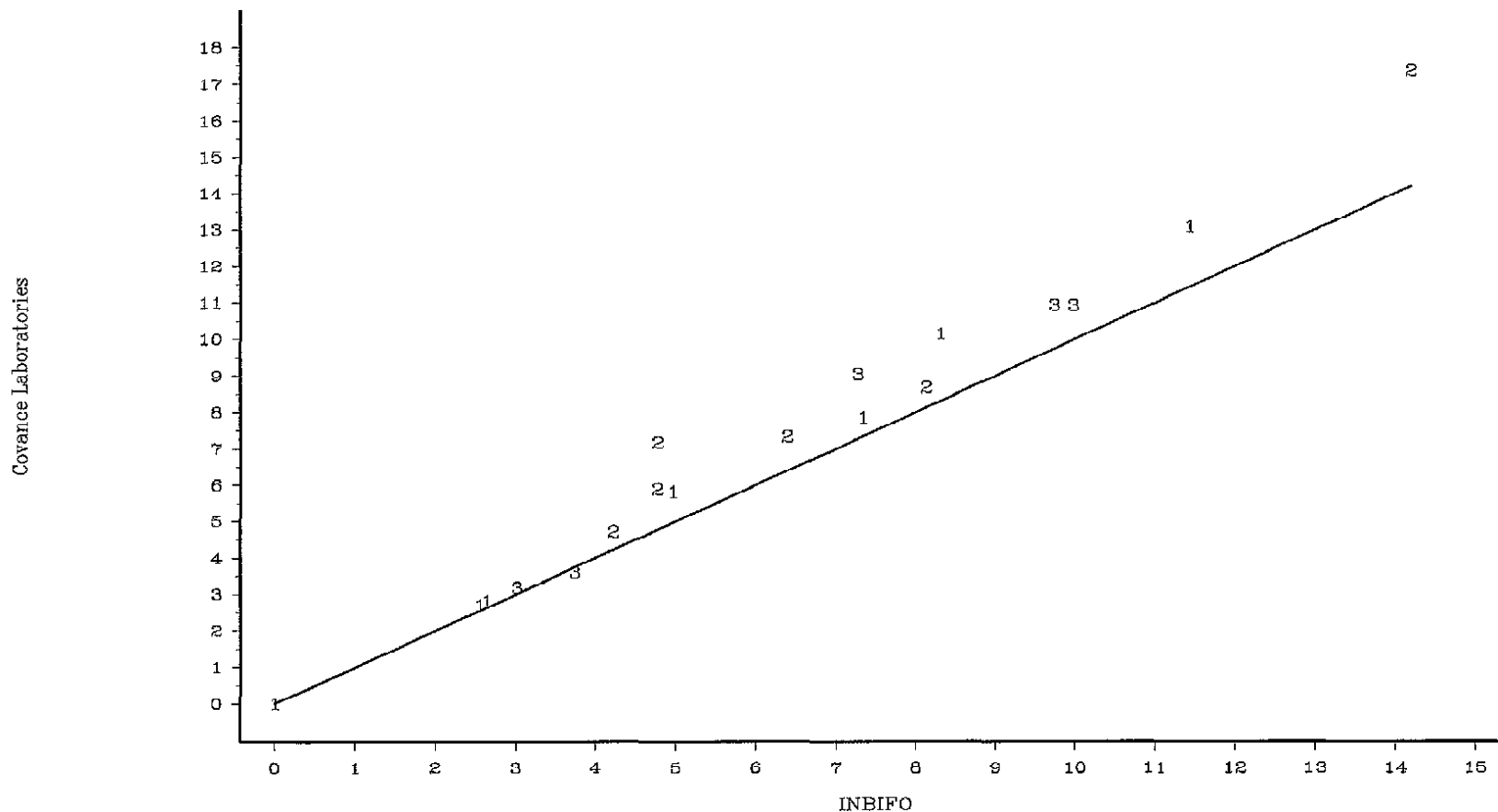
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24-Hour Urine Biomarker of Exposure:
Cotinine (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-4
Covance by INBIFO for Cotinine (nmol/mg Creatinine)

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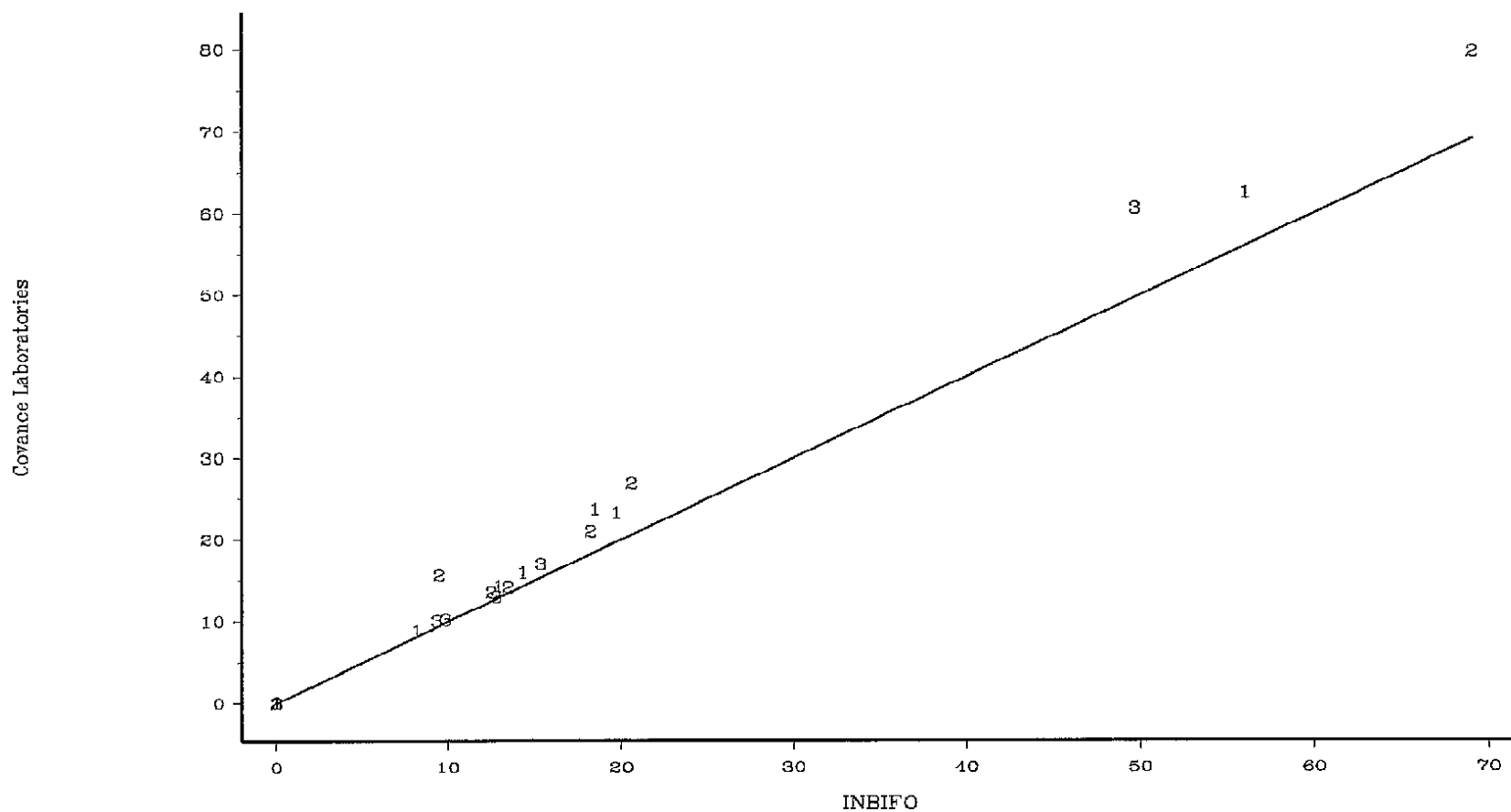
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24-Hour Urine Biomarker of Exposure:
Trans-3-hydroxycotinine (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-5
Covance by INBIFO for Trans-3-hydroxycotinine (nmol/mg Creatinine)

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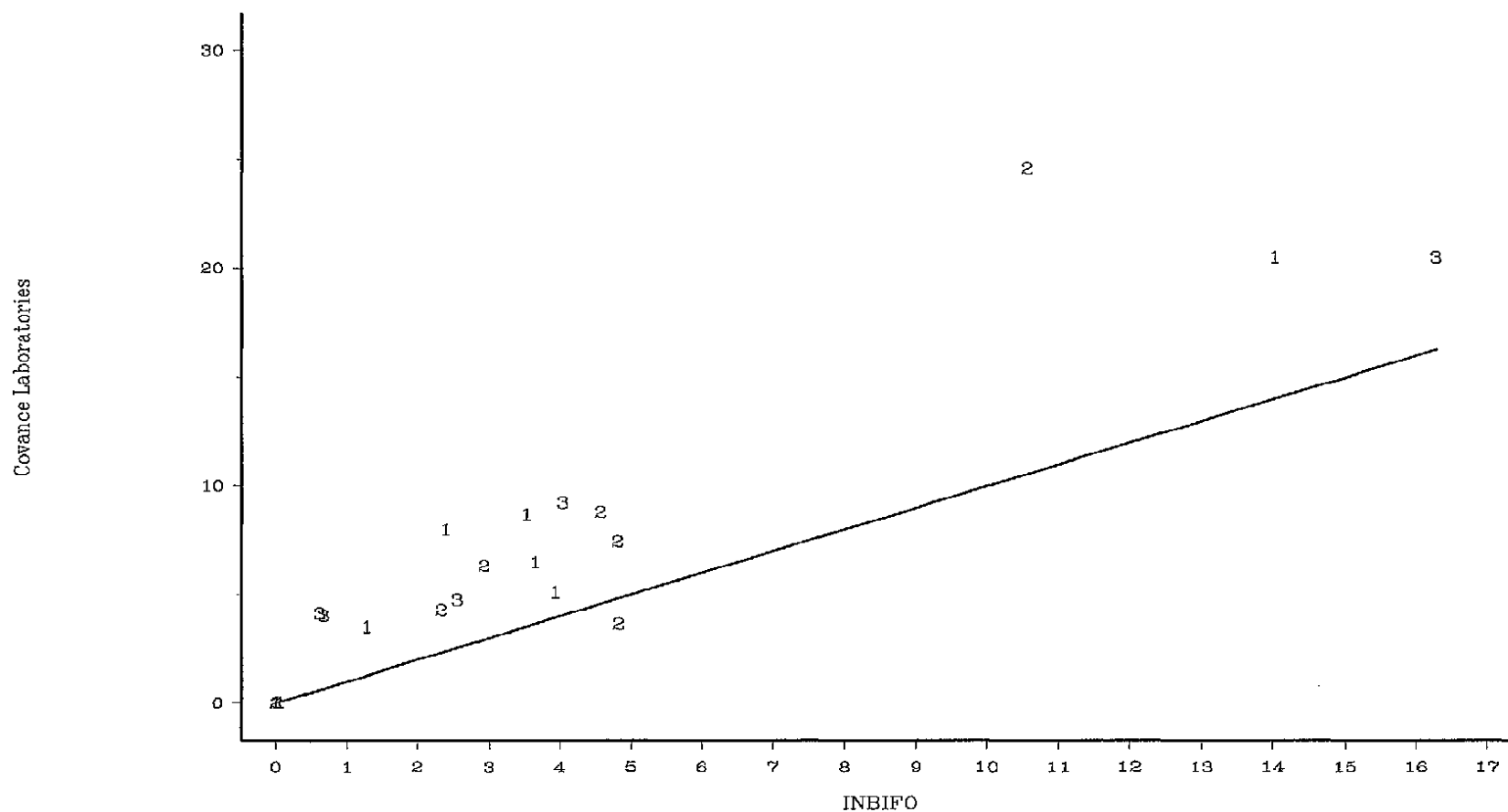
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24-Hour Urine Biomarker of Exposure:
Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-6
Covance by INBIFO for Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)

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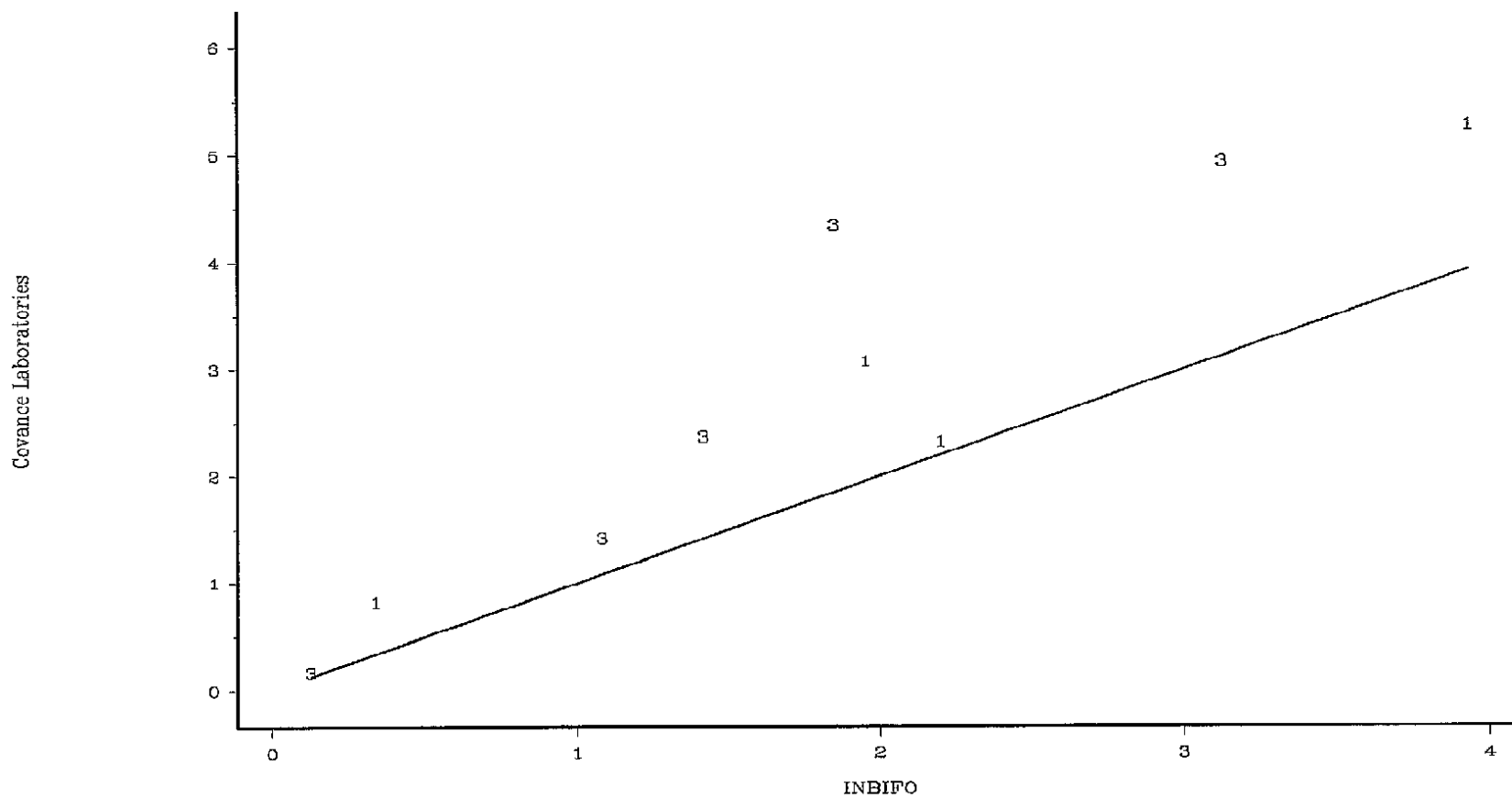
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24-Hour Urine Biomarker of Exposure:
NNAL plus NNAL-gluc (pmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 3=Week 3

Figure 14.1.4.1-7
Covance by INBIFO for NNAL plus NNAL-gluc (pmol/mg Creatinine)

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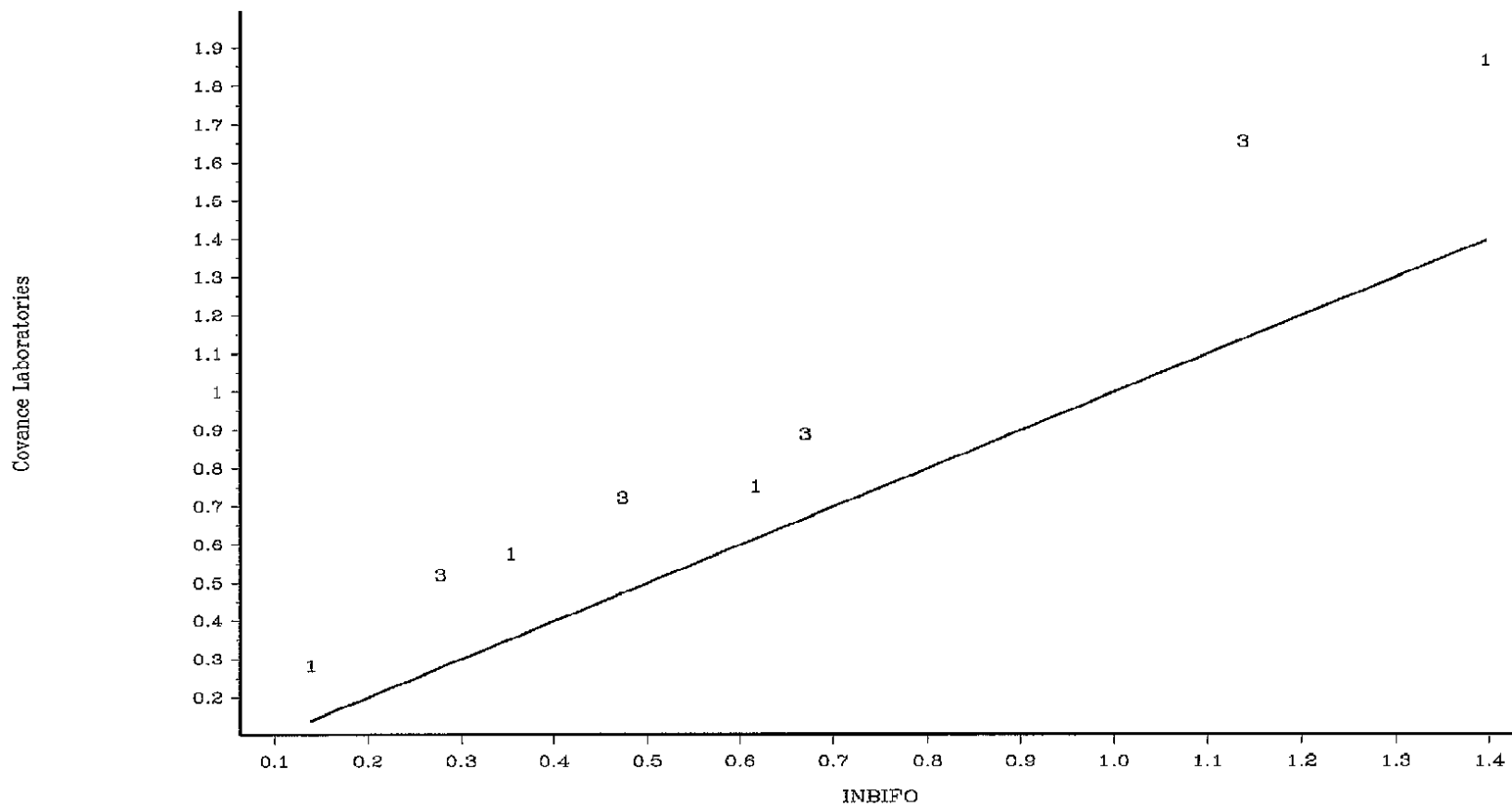
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24-Hour Urine Biomarker of Exposure:
NNAL (pmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 3=Week 3

Figure 14.1.4.1-8
Covance by INBIFO for NNAL (pmol/mg Creatinine)

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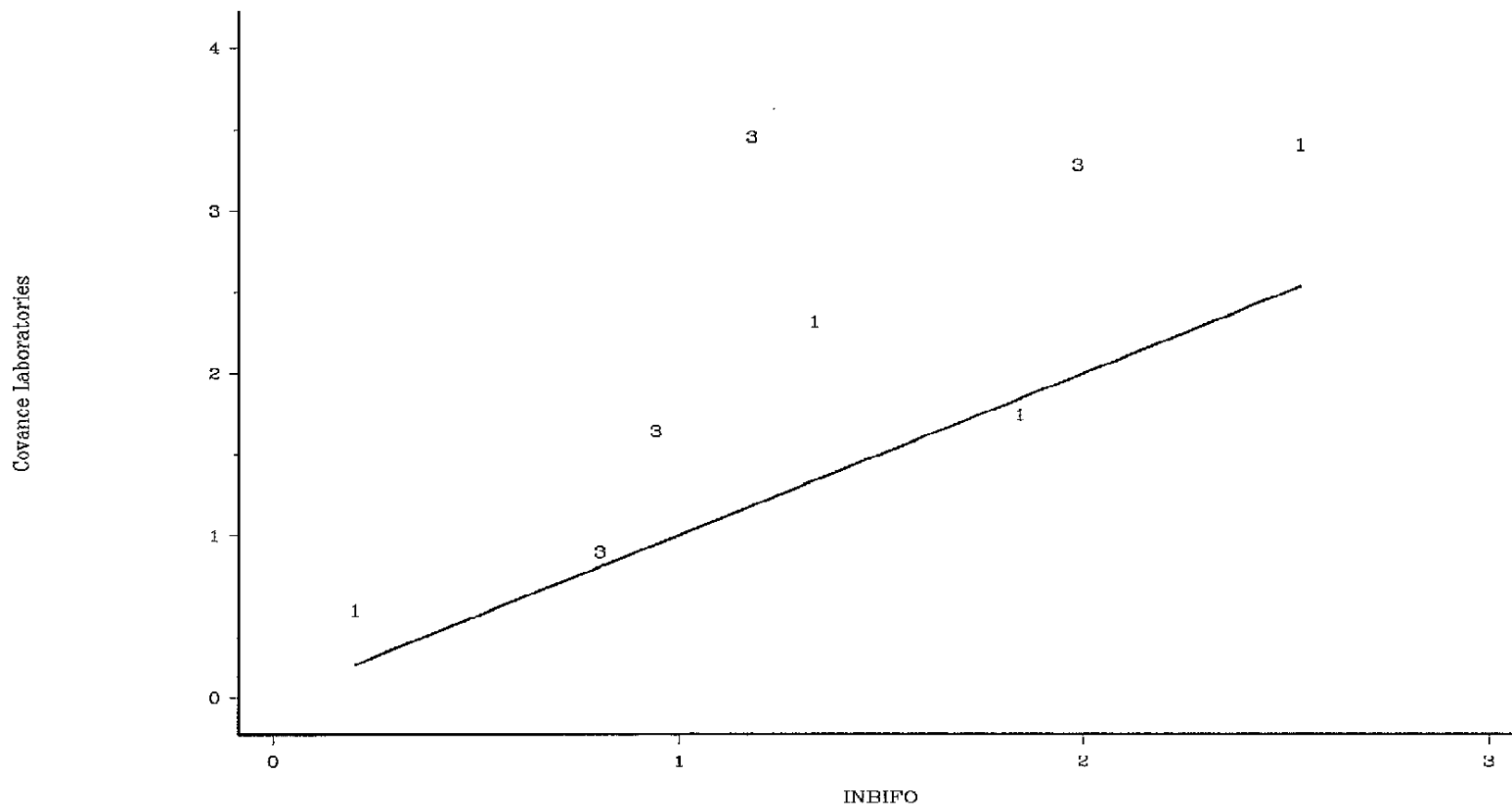
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24-Hour Urine Biomarker of Exposure:
NNAL-O-glucuronide (pmol/mg Creatinine)

Diagonal line is $y=x$.
DLQ values were removed from this analysis.



1=Week 1; 3=Week 3

Figure 14.1.4.1-9
Covance by INBIFO for NNAL-O-glucuronide (pmol/mg Creatinine)

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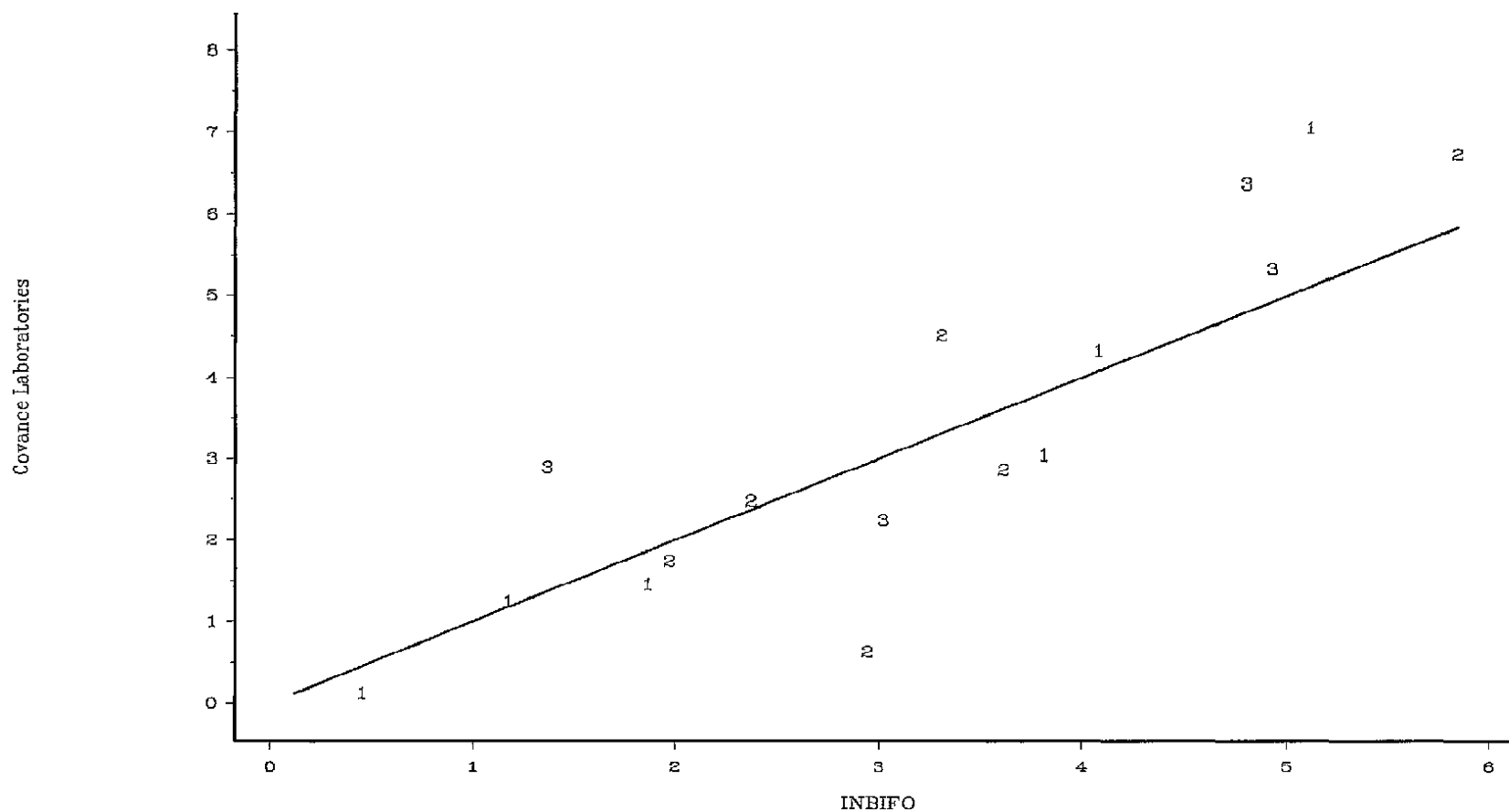
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Protocol No. PM-8450

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24-Hour Urine Biomarker of Exposure:
Nicotine-N-glucuronide (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.



1=Week 1; 2=Week 2; 3=Week 3

Figure 14.1.4.1-10
Covance by INBIFO for Nicotine-N-glucuronide (nmol/mg Creatinine)

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24-Hour Urine Biomarker of Exposure:
Cotinine-N-glucuronide (nmol/mg Creatinine)

Diagonal line is $y=x$.
BLQ values were removed from this analysis.

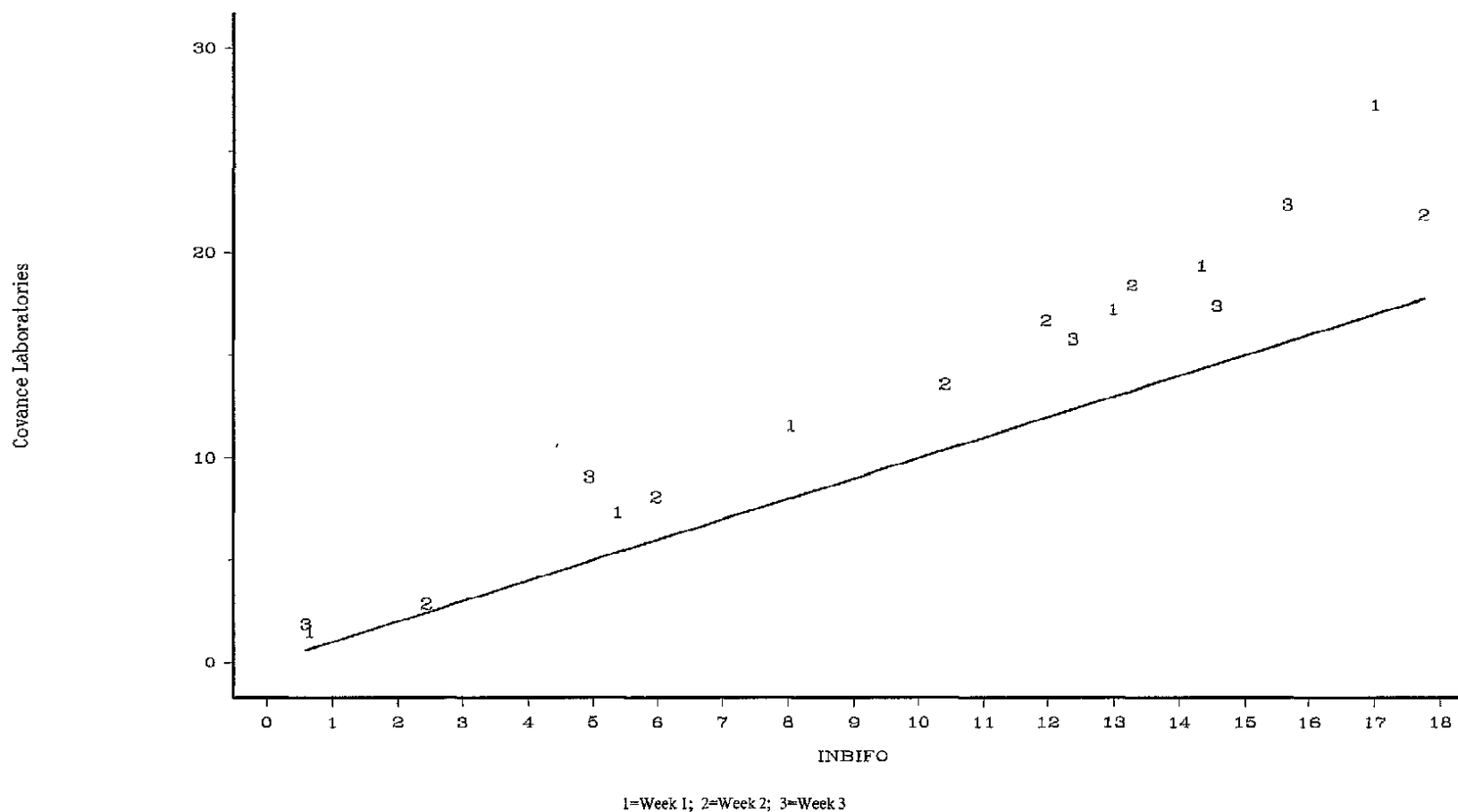


Figure 14.1.4.1-11
Covance by INBIFO for Cotinine-N-glucuronide (nmol/mg Creatinine)

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14.1.4.2 Comparison Between ETS Exposed and Not Exposed Non-Smokers

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
(Page 1 of 7)

Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value ^a
Week 1	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	N	30	35	0.0032
		MEAN, GEO MEAN	8.73, 7.91	6.04, 5.51	
		SD, SE	4.248, 0.776	2.668, 0.451	
		MEDIAN	7.56	5.50	
		MIN, MAX	2.95, 23.25	2.49, 13.38	
		5%, 95%	3.94, 17.37	2.90, 11.63	
		# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	N	30	35	0.0040
		MEAN, GEO MEAN	0.101, 0.053	0.048, NA	
		SD, SE	0.1522, 0.0278	0.0739, 0.0125	
		MEDIAN	0.044	0.033	
		MIN, MAX	0.005, 0.677	0.000, 0.340	
		5%, 95%	0.017, 0.447	0.016, 0.306	
		# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	N	30	35	0.4031
		MEAN, GEO MEAN	0.028, NA	0.013, NA	
		SD, SE	0.0644, 0.0118	0.0174, 0.0029	
		MEDIAN	0.012	0.006	
		MIN, MAX	0.000, 0.271	0.000, 0.086	
		5%, 95%	0.000, 0.253	0.000, 0.074	
		# of BLQ/ALQ Values	19/0	32/0	
	Harrogate Cotinine (nmol/mg Creatinine)	N	30	35	0.4254
		MEAN, GEO MEAN	0.016, NA	0.011, NA	
		SD, SE	0.0220, 0.0040	0.0118, 0.0020	
		MEDIAN	0.011	0.006	
		MIN, MAX	0.000, 0.114	0.000, 0.057	
		5%, 95%	0.000, 0.057	0.000, 0.051	
		# of BLQ/ALQ Values	18/0	31/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value ^a
Week 1	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	N	30	35	0.0073
		MEAN, GEO MEAN	0.035, 0.019	0.017, NA	
		SD, SE	0.0497, 0.0091	0.0320, 0.0054	
		MEDIAN	0.016	0.010	
		MIN, MAX	0.005, 0.219	0.000, 0.187	
		5%, 95%	0.005, 0.166	0.005, 0.068	
		# of BLQ/ALQ Values	8/0	14/0	
	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	N	28	25	0.0284
		MEAN, GEO MEAN	0.009, NA	0.002, NA	
		SD, SE	0.0145, 0.0027	0.0044, 0.0009	
		MEDIAN	0.003	0.001	
		MIN, MAX	0.000, 0.053	0.000, 0.018	
		5%, 95%	0.000, 0.051	0.000, 0.012	
		# of BLQ/ALQ Values	8/0	14/0	
	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	N	29	33	0.0158
		MEAN, GEO MEAN	0.003, NA	0.001, NA	
		SD, SE	0.0047, 0.0009	0.0048, 0.0008	
		MEDIAN	0.000	0.000	
		MIN, MAX	0.000, 0.021	0.000, 0.023	
		5%, 95%	0.000, 0.012	0.000, 0.016	
		# of BLQ/ALQ Values	19/0	32/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	N	30	35	0.0012
		MEAN, GEO MEAN	0.012, NA	0.005, NA	
		SD, SE	0.0200, 0.0037	0.0143, 0.0024	
		MEDIAN	0.004	0.000	
		MIN, MAX	0.000, 0.075	0.000, 0.064	
		5%, 95%	0.000, 0.066	0.000, 0.055	
		# of BLQ/ALQ Values	18/0	31/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value*
Week 2	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	N	28	37	<.0001
		MEAN, GEO MEAN	0.212, 0.086	0.036, NA	
		SD, SE	0.5467, 0.1033	0.0345, 0.0057	
		MEDIAN	0.077	0.022	
		MIN, MAX	0.016, 2.938	0.000, 0.186	
		5%, 95%	0.017, 0.606	0.011, 0.105	
		# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	N	28	37	0.0064
		MEAN, GEO MEAN	0.079, NA	0.009, NA	
		SD, SE	0.3342, 0.0632	0.0063, 0.0010	
		MEDIAN	0.012	0.006	
		MIN, MAX	0.000, 1.782	0.000, 0.025	
		5%, 95%	0.006, 0.086	0.000, 0.025	
		# of BLQ/ALQ Values	18/0	36/0	
	Harrogate Cotinine (nmol/mg Creatinine)	N	28	37	0.0008
		MEAN, GEO MEAN	0.027, NA	0.009, NA	
		SD, SE	0.0590, 0.0112	0.0071, 0.0012	
		MEDIAN	0.011	0.006	
		MIN, MAX	0.000, 0.323	0.000, 0.028	
		5%, 95%	0.006, 0.040	0.000, 0.028	
		# of BLQ/ALQ Values	12/0	35/0	
	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	N	28	37	<.0001
		MEAN, GEO MEAN	0.059, 0.028	0.013, NA	
		SD, SE	0.0910, 0.0172	0.0117, 0.0019	
		MEDIAN	0.024	0.010	
		MIN, MAX	0.005, 0.411	0.000, 0.062	
		5%, 95%	0.005, 0.297	0.005, 0.036	
		# of BLQ/ALQ Values	6/0	11/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

* P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value ^a
Week 2	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	N	26	33	0.0061
		MEAN, GEO MEAN	0.017, NA	0.003, NA	
		SD, SE	0.0260, 0.0051	0.0051, 0.0009	
		MEDIAN	0.005	0.001	
		MIN, MAX	0.000, 0.105	0.000, 0.021	
		5%, 95%	0.000, 0.072	0.000, 0.016	
		# of BLQ/ALQ Values	6/0	11/0	
	Harrogate Nicotine-N-glucuronide (amol/mg Creatinine)	N	26	37	0.0001
		MEAN, GEO MEAN	0.013, NA	0.000, NA	
		SD, SE	0.0526, 0.0103	0.0013, 0.0002	
		MEDIAN	0.000	0.000	
		MIN, MAX	0.000, 0.270	0.000, 0.008	
		5%, 95%	0.000, 0.017	0.000, 0.000	
		# of BLQ/ALQ Values	18/0	36/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	N	28	37	<.0001
		MEAN, GEO MEAN	0.021, NA	0.003, NA	
		SD, SE	0.0371, 0.0070	0.0107, 0.0018	
		MEDIAN	0.012	0.000	
		MIN, MAX	0.000, 0.195	0.000, 0.058	
		5%, 95%	0.000, 0.045	0.000, 0.026	
		# of BLQ/ALQ Values	12/0	35/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value*
Week 3	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	N	17	48	0.0057
		MEAN, GEO MEAN	0.104, 0.066	0.040, 0.032	
		SD, SE	0.1163, 0.0282	0.0404, 0.0058	
		MEDIAN	0.069	0.033	
		MIN, MAX	0.016, 0.470	0.011, 0.274	
		5%, 95%	0.016, 0.470	0.017, 0.085	
		# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	N	17	48	0.9172
		MEAN, GEO MEAN	0.011, NA	0.010, NA	
		SD, SE	0.0110, 0.0027	0.0062, 0.0009	
		MEDIAN	0.012	0.006	
		MIN, MAX	0.000, 0.049	0.000, 0.031	
		5%, 95%	0.000, 0.049	0.006, 0.025	
		# of BLQ/ALQ Values	12/0	45/0	
	Harrogate Cotinine (nmol/mg Creatinine)	N	17	48	0.1767
		MEAN, GEO MEAN	0.017, NA	0.010, NA	
		SD, SE	0.0198, 0.0048	0.0079, 0.0011	
		MEDIAN	0.011	0.006	
		MIN, MAX	0.000, 0.079	0.000, 0.051	
		5%, 95%	0.000, 0.079	0.006, 0.023	
		# of BLQ/ALQ Values	7/0	43/0	
	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	N	17	48	0.0031
		MEAN, GEO MEAN	0.043, 0.024	0.014, 0.010	
		SD, SE	0.0538, 0.0130	0.0153, 0.0022	
		MEDIAN	0.026	0.010	
		MIN, MAX	0.005, 0.213	0.005, 0.094	
		5%, 95%	0.005, 0.213	0.005, 0.042	
		# of BLQ/ALQ Values	0/0	30/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

* P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value ^a
Week 3	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	N	15	46	<.0001
		MEAN, GEO MEAN	0.013, NA	0.002, NA	
		SD, SE	0.0147, 0.0038	0.0063, 0.0009	
		MEDIAN	0.009	0.000	
		MIN, MAX	0.000, 0.050	0.000, 0.040	
		5%, 95%	0.000, 0.050	0.000, 0.008	
		# of BLQ/ALQ Values	0/0	30/0	
	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	N	17	48	0.0002
		MEAN, GEO MEAN	0.004, NA	0.000, NA	
		SD, SE	0.0055, 0.0013	0.0017, 0.0002	
		MEDIAN	0.002	0.000	
		MIN, MAX	0.000, 0.021	0.000, 0.008	
		5%, 95%	0.000, 0.021	0.000, 0.003	
		# of BLQ/ALQ Values	12/0	45/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	N	17	48	<.0001
		MEAN, GEO MEAN	0.017, NA	0.003, NA	
		SD, SE	0.0199, 0.0048	0.0097, 0.0014	
		MEDIAN	0.011	0.000	
		MIN, MAX	0.000, 0.067	0.000, 0.060	
		5%, 95%	0.000, 0.067	0.000, 0.015	
		# of BLQ/ALQ Values	7/0	43/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-1
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value*
Week 6	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	N	23	42	0.5974
		MEAN, GEO MEAN	9.45, 8.35	8.46, 7.75	
		SD, SE	5.727, 1.194	3.807, 0.587	
		MEDIAN	7.37	7.52	
		MIN, MAX	4.31, 27.86	4.09, 20.64	
		5%, 95%	4.49, 22.67	4.36, 15.32	
		# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

* P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-2
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Month Period Before Sample Collection at Enrollment
(Page 1 of 2)

Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value ^a
Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	N	28	37	0.0627
	MEAN, GEO MEAN	7.89, 7.25	6.82, 6.01	
	SD, SE	3.182, 0.601	4.050, 0.666	
	MEDIAN	7.56	6.22	
	MIN, MAX	2.95, 13.87	2.49, 23.25	
	5%, 95%	3.94, 13.59	2.90, 17.37	
	# of BLQ/ALQ Values	0/0	0/0	
Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	N	28	37	0.0021
	MEAN, GEO MEAN	0.126, 0.062	0.033, NA	
	SD, SE	0.1656, 0.0313	0.0266, 0.0044	
	MEDIAN	0.047	0.033	
	MIN, MAX	0.005, 0.677	0.000, 0.173	
	5%, 95%	0.016, 0.447	0.017, 0.051	
	# of BLQ/ALQ Values	0/0	0/0	
Harrogate Nicotine (nmol/mg Creatinine)	N	28	37	0.3843
	MEAN, GEO MEAN	0.034, NA	0.009, NA	
	SD, SE	0.0678, 0.0128	0.0044, 0.0007	
	MEDIAN	0.009	0.006	
	MIN, MAX	0.000, 0.271	0.000, 0.018	
	5%, 95%	0.000, 0.253	0.000, 0.018	
	# of BLQ/ALQ Values	16/0	35/0	
Harrogate Cotinine (nmol/mg Creatinine)	N	28	37	0.3676
	MEAN, GEO MEAN	0.019, NA	0.009, NA	
	SD, SE	0.0249, 0.0047	0.0051, 0.0008	
	MEDIAN	0.009	0.006	
	MIN, MAX	0.000, 0.114	0.000, 0.028	
	5%, 95%	0.000, 0.057	0.000, 0.017	
	# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-2
Statistical Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke Within 3-Month Period Before Sample Collection at Enrollment
(Page 2 of 2)

Analytical Lab Biomarker	Statistic	Exposed	Not-exposed	P-value*
Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	N	28	37	0.0004
	MEAN, GEO MEAN	0.045, 0.023	0.011, NA	
	SD, SE	0.0580, 0.0110	0.0075, 0.0012	
	MEDIAN	0.019	0.010	
	MIN, MAX	0.005, 0.219	0.000, 0.042	
	5%, 95%	0.005, 0.187	0.005, 0.026	
	# of BLQ/ALQ Values	4/0	18/0	
Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	N	25	28	<.0001
	MEAN, GEO MEAN	0.011, NA	0.002, NA	
	SD, SE	0.0147, 0.0029	0.0036, 0.0007	
	MEDIAN	0.006	0.000	
	MIN, MAX	0.000, 0.053	0.000, 0.015	
	5%, 95%	0.000, 0.051	0.000, 0.012	
	# of BLQ/ALQ Values	4/0	18/0	
Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	N	26	36	0.0021
	MEAN, GEO MEAN	0.004, NA	0.001, NA	
	SD, SE	0.0063, 0.0012	0.0028, 0.0005	
	MEDIAN	0.000	0.000	
	MIN, MAX	0.000, 0.023	0.000, 0.016	
	5%, 95%	0.000, 0.021	0.000, 0.004	
	# of BLQ/ALQ Values	16/0	35/0	
Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	N	28	37	<.0001
	MEAN, GEO MEAN	0.016, NA	0.002, NA	
	SD, SE	0.0223, 0.0042	0.0091, 0.0015	
	MEDIAN	0.008	0.000	
	MIN, MAX	0.000, 0.075	0.000, 0.055	
	5%, 95%	0.000, 0.066	0.000, 0.007	
	# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

* P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 1 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Spouse at home	N	2	63	0.1656
			MEAN, GEO MEAN	9.17, 9.15	7.22, 6.44	
			SD, SE	0.856, 0.605	3.755, 0.473	
			MEDIAN	9.17	6.54	
			MIN, MAX	8.56, 9.77	2.49, 23.25	
			5%, 95%	8.56, 9.77	3.12, 13.59	
			# of BLQ/ALQ Values	0/0	0/0	
		Others at home	N	5	60	0.0518
			MEAN, GEO MEAN	9.81, 9.42	7.07, 6.32	
			SD, SE	3.126, 1.398	3.701, 0.478	
			MEDIAN	9.43	6.52	
			MIN, MAX	6.76, 13.87	2.49, 23.25	
			5%, 95%	6.76, 13.87	3.04, 13.49	
			# of BLQ/ALQ Values	0/0	0/0	
		At home combined	N	7	58	0.0141
			MEAN, GEO MEAN	9.63, 9.34	7.00, 6.24	
			SD, SE	2.595, 0.981	3.743, 0.491	
			MEDIAN	9.43	6.37	
			MIN, MAX	6.76, 13.87	2.49, 23.25	
			5%, 95%	6.76, 13.87	2.95, 13.59	
			# of BLQ/ALQ Values	0/0	0/0	
		Work	N	4	61	0.8165
			MEAN, GEO MEAN	8.04, 6.86	7.23, 6.49	
			SD, SE	4.788, 2.394	3.676, 0.471	
			MEDIAN	7.82	6.55	
			MIN, MAX	2.95, 13.59	2.49, 23.25	
			5%, 95%	2.95, 13.59	3.21, 13.38	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 2 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Vehicles	N	2	63	0.4141
			MEAN, GEO MEAN	5.42, 5.42	7.34, 6.55	
			SD, SE	0.071, 0.050	3.757, 0.473	
			MEDIAN	5.42	6.76	
			MIN, MAX	5.37, 5.47	2.49, 23.25	
			5%, 95%	5.37, 5.47	3.12, 13.59	
			# of BLQ/ALQ Values	0/0	0/0	
		Other places	N	21	44	0.0109
			MEAN, GEO MEAN	9.13, 8.27	6.39, 5.81	
			SD, SE	4.624, 1.009	2.843, 0.429	
			MEDIAN	7.59	6.22	
			MIN, MAX	3.94, 23.25	2.49, 13.87	
			5%, 95%	4.65, 17.37	2.95, 11.63	
			# of BLQ/ALQ Values	0/0	0/0	
		Away from home combined	N	25	40	0.0411
			MEAN, GEO MEAN	8.64, 7.74	6.43, 5.85	
			SD, SE	4.512, 0.902	2.859, 0.452	
			MEDIAN	7.53	6.38	
			MIN, MAX	2.95, 23.25	2.49, 13.87	
			5%, 95%	3.94, 17.37	3.01, 12.51	
			# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0331
			MEAN, GEO MEAN	0.308, 0.275	0.065, NA	
			SD, SE	0.1966, 0.1390	0.1100, 0.0139	
			MEDIAN	0.308	0.033	
			MIN, MAX	0.169, 0.447	0.000, 0.677	
			5%, 95%	0.169, 0.447	0.017, 0.306	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Others at home	N	5	60	0.2960
			MEAN, GEO MEAN	0.180, 0.074	0.064, NA	
			SD, SE	0.2812, 0.1257	0.0944, 0.0122	
			MEDIAN	0.045	0.033	
			MIN, MAX	0.017, 0.677	0.000, 0.447	
			5%, 95%	0.017, 0.677	0.017, 0.323	
			# of BLQ/ALQ Values	0/0	0/0	
		At home combined	N	7	58	0.0361
			MEAN, GEO MEAN	0.216, 0.107	0.056, NA	
			SD, SE	0.2511, 0.0949	0.0799, 0.0105	
			MEDIAN	0.127	0.033	
			MIN, MAX	0.017, 0.677	0.000, 0.430	
			5%, 95%	0.017, 0.677	0.016, 0.306	
			# of BLQ/ALQ Values	0/0	0/0	
		Work	N	4	61	0.0774
			MEAN, GEO MEAN	0.082, 0.073	0.072, NA	
			SD, SE	0.0428, 0.0214	0.1223, 0.0157	
			MEDIAN	0.080	0.033	
			MIN, MAX	0.033, 0.136	0.000, 0.677	
			5%, 95%	0.033, 0.136	0.017, 0.340	
			# of BLQ/ALQ Values	0/0	0/0	
		Vehicles	N	2	63	0.1446
			MEAN, GEO MEAN	0.061, 0.060	0.073, NA	
			SD, SE	0.0141, 0.0100	0.1207, 0.0152	
			MEDIAN	0.061	0.033	
			MIN, MAX	0.051, 0.071	0.000, 0.677	
			5%, 95%	0.051, 0.071	0.017, 0.340	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Other places	N	21	44	0.1091
			MEAN, GEO MEAN	0.097, 0.048	0.061, NA	
			SD, SE	0.1618, 0.0353	0.0917, 0.0138	
			MEDIAN	0.043	0.033	
			MIN, MAX	0.005, 0.677	0.000, 0.447	
			5%, 95%	0.017, 0.430	0.017, 0.306	
			# of BLQ/ALQ Values	0/0	0/0	
		Away from home combined	N	25	40	0.0184
			MEAN, GEO MEAN	0.093, 0.050	0.060, NA	
			SD, SE	0.1488, 0.0298	0.0954, 0.0151	
			MEDIAN	0.043	0.033	
			MIN, MAX	0.005, 0.677	0.000, 0.447	
			5%, 95%	0.017, 0.430	0.017, 0.323	
			# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0271
			MEAN, GEO MEAN	0.043, 0.041	0.019, NA	
			SD, SE	0.0170, 0.0120	0.0463, 0.0058	
			MEDIAN	0.043	0.006	
			MIN, MAX	0.031, 0.055	0.000, 0.271	
			5%, 95%	0.031, 0.055	0.000, 0.074	
			# of BLQ/ALQ Values	0/0	51/0	
		Others at home	N	5	60	0.5195
			MEAN, GEO MEAN	0.058, 0.017	0.017, NA	
			SD, SE	0.1092, 0.0488	0.0366, 0.0047	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.006, 0.253	0.000, 0.271	
			5%, 95%	0.006, 0.253	0.000, 0.065	
			# of BLQ/ALQ Values	3/0	48/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Nicotine (nmol/mg Creatinine)	At home combined	N	7	58	0.0724
			MEAN, GEO MEAN	0.054, 0.022	0.016, NA	
			SD, SE	0.0897, 0.0339	0.0368, 0.0048	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.006, 0.253	0.000, 0.271	
			5%, 95%	0.006, 0.253	0.000, 0.074	
			# of BLQ/ALQ Values	3/0	48/0	
		Work	N	4	61	0.8497
			MEAN, GEO MEAN	0.011, 0.009	0.020, NA	
			SD, SE	0.0057, 0.0029	0.0473, 0.0061	
			MEDIAN	0.009	0.006	
			MIN, MAX	0.006, 0.018	0.000, 0.271	
			5%, 95%	0.006, 0.018	0.000, 0.074	
			# of BLQ/ALQ Values	1/0	50/0	
		Vehicles	N	2	63	0.7000
			MEAN, GEO MEAN	0.012, 0.010	0.020, NA	
			SD, SE	0.0085, 0.0060	0.0466, 0.0059	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.006, 0.018	0.000, 0.271	
			5%, 95%	0.006, 0.018	0.000, 0.074	
			# of BLQ/ALQ Values	1/0	50/0	
		Other places	N	21	44	0.8281
			MEAN, GEO MEAN	0.033, NA	0.014, NA	
			SD, SE	0.0764, 0.0167	0.0171, 0.0026	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.000, 0.271	0.000, 0.086	
			5%, 95%	0.000, 0.253	0.006, 0.055	
			# of BLQ/ALQ Values	14/0	37/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Nicotine (nmol/mg Creatinine)	Away from home combined	N	25	40	0.7569
			MEAN, GEO MEAN	0.029, NA	0.014, NA	
			SD, SE	0.0702, 0.0140	0.0179, 0.0028	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.000, 0.271	0.000, 0.086	
			5%, 95%	0.000, 0.253	0.003, 0.065	
			# of BLQ/ALQ Values	16/0	35/0	
	Harrogate Cotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0308
			MEAN, GEO MEAN	0.034, 0.032	0.013, NA	
			SD, SE	0.0156, 0.0110	0.0170, 0.0021	
			MEDIAN	0.034	0.006	
			MIN, MAX	0.023, 0.045	0.000, 0.114	
			5%, 95%	0.023, 0.045	0.000, 0.051	
			# of BLQ/ALQ Values	0/0	49/0	
		Others at home	N	5	60	0.5387
			MEAN, GEO MEAN	0.030, 0.014	0.012, NA	
			SD, SE	0.0472, 0.0211	0.0122, 0.0016	
			MEDIAN	0.011	0.006	
			MIN, MAX	0.006, 0.114	0.000, 0.057	
			5%, 95%	0.006, 0.114	0.000, 0.048	
			# of BLQ/ALQ Values	3/0	46/0	
		At home combined	N	7	58	0.0813
			MEAN, GEO MEAN	0.031, 0.018	0.011, NA	
			SD, SE	0.0392, 0.0148	0.0115, 0.0015	
			MEDIAN	0.011	0.006	
			MIN, MAX	0.006, 0.114	0.000, 0.057	
			5%, 95%	0.006, 0.114	0.000, 0.051	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Cotinine (nmol/mg Creatinine)	Work	N	4	61	0.9076
			MEAN, GEO MEAN	0.010, 0.009	0.013, NA	
			SD, SE	0.0052, 0.0026	0.0178, 0.0023	
			MEDIAN	0.009	0.006	
			MIN, MAX	0.006, 0.017	0.000, 0.114	
			5%, 95%	0.006, 0.017	0.000, 0.051	
			# of BLQ/ALQ Values	1/0	48/0	
		Vehicles	N	2	63	0.7467
			MEAN, GEO MEAN	0.012, 0.010	0.013, NA	
			SD, SE	0.0078, 0.0055	0.0175, 0.0022	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.006, 0.017	0.000, 0.114	
			5%, 95%	0.006, 0.017	0.000, 0.051	
			# of BLQ/ALQ Values	1/0	48/0	
		Other places	N	21	44	0.7770
			MEAN, GEO MEAN	0.015, NA	0.012, NA	
			SD, SE	0.0253, 0.0055	0.0119, 0.0018	
			MEDIAN	0.006	0.009	
			MIN, MAX	0.000, 0.114	0.000, 0.057	
			5%, 95%	0.000, 0.057	0.006, 0.045	
			# of BLQ/ALQ Values	13/0	36/0	
		Away from home combined	N	25	40	0.7635
			MEAN, GEO MEAN	0.015, NA	0.012, NA	
			SD, SE	0.0232, 0.0046	0.0125, 0.0020	
			MEDIAN	0.011	0.006	
			MIN, MAX	0.000, 0.114	0.000, 0.057	
			5%, 95%	0.000, 0.057	0.003, 0.048	
			# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0228
			MEAN, GEO MEAN	0.149, 0.131	0.022, NA	
			SD, SE	0.0997, 0.0705	0.0338, 0.0043	
			MEDIAN	0.149	0.010	
			MIN, MAX	0.078, 0.219	0.000, 0.187	
			5%, 95%	0.078, 0.219	0.005, 0.083	
			# of BLQ/ALQ Values	0/0	22/0	
		Others at home	N	5	60	0.3772
			MEAN, GEO MEAN	0.048, 0.022	0.024, NA	
			SD, SE	0.0676, 0.0302	0.0393, 0.0051	
			MEDIAN	0.016	0.010	
			MIN, MAX	0.005, 0.166	0.000, 0.219	
			5%, 95%	0.005, 0.166	0.005, 0.091	
			# of BLQ/ALQ Values	1/0	21/0	
		At home combined	N	7	58	0.0415
			MEAN, GEO MEAN	0.077, 0.037	0.019, NA	
			SD, SE	0.0844, 0.0319	0.0293, 0.0038	
			MEDIAN	0.042	0.010	
			MIN, MAX	0.005, 0.219	0.000, 0.187	
			5%, 95%	0.005, 0.219	0.005, 0.083	
			# of BLQ/ALQ Values	1/0	21/0	
		Work	N	4	61	0.0828
			MEAN, GEO MEAN	0.032, 0.027	0.025, NA	
			SD, SE	0.0218, 0.0109	0.0429, 0.0055	
			MEDIAN	0.029	0.010	
			MIN, MAX	0.010, 0.062	0.000, 0.219	
			5%, 95%	0.010, 0.062	0.005, 0.099	
			# of BLQ/ALQ Values	1/0	21/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Vehicles	N	2	63	0.2201
			MEAN, GEO MEAN	0.024, 0.022	0.026, NA	
			SD, SE	0.0106, 0.0075	0.0425, 0.0053	
			MEDIAN	0.024	0.010	
			MIN, MAX	0.016, 0.031	0.000, 0.219	
			5%, 95%	0.016, 0.031	0.005, 0.099	
			# of BLQ/ALQ Values	1/0	21/0	
		Other places	N	21	44	0.1276
			MEAN, GEO MEAN	0.029, 0.017	0.024, NA	
			SD, SE	0.0398, 0.0087	0.0431, 0.0065	
			MEDIAN	0.016	0.010	
			MIN, MAX	0.005, 0.166	0.000, 0.219	
			5%, 95%	0.005, 0.099	0.005, 0.078	
			# of BLQ/ALQ Values	5/0	17/0	
		Away from home combined	N	25	40	0.0290
			MEAN, GEO MEAN	0.029, 0.018	0.023, NA	
			SD, SE	0.0373, 0.0075	0.0447, 0.0071	
			MEDIAN	0.016	0.010	
			MIN, MAX	0.005, 0.166	0.000, 0.219	
			5%, 95%	0.005, 0.099	0.005, 0.133	
			# of BLQ/ALQ Values	7/0	15/0	
	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	51	0.0198
			MEAN, GEO MEAN	0.039, 0.036	0.005, NA	
			SD, SE	0.0198, 0.0140	0.0090, 0.0073	
			MEDIAN	0.039	0.001	
			MIN, MAX	0.025, 0.053	0.000, 0.051	
			5%, 95%	0.025, 0.053	0.000, 0.018	
			# of BLQ/ALQ Values	0/0	22/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Others at home	N	5	48	0.2798
			MEAN, GEO MEAN	0.013, NA	0.005, NA	
			SD, SE	0.0213, 0.0095	0.0099, 0.0014	
			MEDIAN	0.005	0.001	
			MIN, MAX	0.000, 0.051	0.000, 0.053	
			5%, 95%	0.000, 0.051	0.000, 0.025	
			# of BLQ/ALQ Values	1/0	21/0	
		At home combined	N	7	46	0.0239
			MEAN, GEO MEAN	0.021, NA	0.004, NA	
			SD, SE	0.0230, 0.0087	0.0064, 0.0009	
			MEDIAN	0.008	0.001	
			MIN, MAX	0.000, 0.053	0.000, 0.034	
			5%, 95%	0.000, 0.053	0.000, 0.015	
			# of BLQ/ALQ Values	1/0	21/0	
		Work	N	4	49	0.2825
			MEAN, GEO MEAN	0.007, NA	0.006, NA	
			SD, SE	0.0050, 0.0025	0.0118, 0.0017	
			MEDIAN	0.009	0.001	
			MIN, MAX	0.000, 0.011	0.000, 0.053	
			5%, 95%	0.000, 0.011	0.000, 0.034	
			# of BLQ/ALQ Values	1/0	21/0	
		Vehicles	N	2	51	0.9617
			MEAN, GEO MEAN	0.006, NA	0.006, NA	
			SD, SE	0.0078, 0.0055	0.0115, 0.0016	
			MEDIAN	0.006	0.002	
			MIN, MAX	0.000, 0.011	0.000, 0.053	
			5%, 95%	0.000, 0.011	0.000, 0.034	
			# of BLQ/ALQ Values	1/0	21/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure*	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Other places	N	19	34	0.1577
			MEAN, GEO MEAN	0.008, NA	0.005, NA	
			SD, SE	0.0132, 0.0030	0.0102, 0.0018	
			MEDIAN	0.003	0.001	
			MIN, MAX	0.000, 0.051	0.000, 0.053	
			5%, 95%	0.000, 0.051	0.000, 0.025	
			# of BLQ/ALQ Values	5/0	17/0	
		Away from home combined	N	23	30	0.1630
			MEAN, GEO MEAN	0.008, NA	0.005, NA	
			SD, SE	0.0122, 0.0025	0.0107, 0.0020	
			MEDIAN	0.003	0.001	
			MIN, MAX	0.000, 0.051	0.000, 0.053	
			5%, 95%	0.000, 0.034	0.000, 0.025	
			# of BLQ/ALQ Values	7/0	15/0	
	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	60	0.3249
			MEAN, GEO MEAN	0.006, NA	0.002, NA	
			SD, SE	0.0085, 0.0060	0.0047, 0.0006	
			MEDIAN	0.006	0.000	
			MIN, MAX	0.000, 0.012	0.000, 0.023	
			5%, 95%	0.000, 0.012	0.000, 0.013	
			# of BLQ/ALQ Values	0/0	51/0	
		Others at home	N	5	57	0.0040
			MEAN, GEO MEAN	0.007, NA	0.002, NA	
			SD, SE	0.0084, 0.0037	0.0042, 0.0006	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.000, 0.021	0.000, 0.023	
			5%, 95%	0.000, 0.021	0.000, 0.012	
			# of BLQ/ALQ Values	3/0	48/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

* Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	At home combined	N	7	55	0.0024
			MEAN, GEO MEAN	0.007, NA	0.001, NA	
			SD, SE	0.0077, 0.0029	0.0040, 0.0005	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.000, 0.021	0.000, 0.023	
			5%, 95%	0.000, 0.021	0.000, 0.009	
			# of BLQ/ALQ Values	3/0	48/0	
		Work	N	4	58	0.0162
			MEAN, GEO MEAN	0.005, NA	0.002, NA	
			SD, SE	0.0037, 0.0018	0.0048, 0.0006	
			MEDIAN	0.005	0.000	
			MIN, MAX	0.000, 0.009	0.000, 0.023	
			5%, 95%	0.000, 0.009	0.000, 0.016	
			# of BLQ/ALQ Values	1/0	50/0	
		Vehicles	N	2	60	0.4843
			MEAN, GEO MEAN	0.002, NA	0.002, NA	
			SD, SE	0.0028, 0.0020	0.0048, 0.0006	
			MEDIAN	0.002	0.000	
			MIN, MAX	0.000, 0.004	0.000, 0.023	
			5%, 95%	0.000, 0.004	0.000, 0.014	
			# of BLQ/ALQ Values	1/0	50/0	
		Other places	N	20	42	0.3227
			MEAN, GEO MEAN	0.002, NA	0.002, NA	
			SD, SE	0.0051, 0.0011	0.0047, 0.0007	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.021	0.000, 0.023	
			5%, 95%	0.000, 0.015	0.000, 0.012	
			# of BLQ/ALQ Values	14/0	37/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Away from home combined	N	24	38	0.1280
			MEAN, GEO MEAN	0.002, NA	0.002, NA	
			SD, SE	0.0048, 0.0010	0.0048, 0.0008	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.021	0.000, 0.023	
			5%, 95%	0.000, 0.009	0.000, 0.016	
			# of BLQ/ALQ Values	16/0	35/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0334
			MEAN, GEO MEAN	0.038, 0.026	0.007, NA	
			SD, SE	0.0396, 0.0280	0.0161, 0.0020	
			MEDIAN	0.038	0.000	
			MIN, MAX	0.010, 0.066	0.000, 0.075	
			5%, 95%	0.010, 0.066	0.000, 0.049	
			# of BLQ/ALQ Values	0/0	49/0	
		Others at home	N	5	60	0.0681
			MEAN, GEO MEAN	0.027, NA	0.007, NA	
			SD, SE	0.0336, 0.0150	0.0149, 0.0019	
			MEDIAN	0.009	0.000	
		At home combined	N	7	58	0.0057
			MEAN, GEO MEAN	0.030, NA	0.006, NA	
			SD, SE	0.0323, 0.0122	0.0129, 0.0017	
			MEDIAN	0.010	0.000	
			MIN, MAX	0.000, 0.075	0.000, 0.064	
			5%, 95%	0.000, 0.075	0.000, 0.036	
			# of BLQ/ALQ Values	3/0	46/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 1	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Work	N	4	61	0.0876
			MEAN, GEO MEAN	0.017, NA	0.008, NA	
			SD, SE	0.0156, 0.0078	0.0175, 0.0022	
			MEDIAN	0.017	0.000	
			MIN, MAX	0.000, 0.036	0.000, 0.075	
			5%, 95%	0.000, 0.036	0.000, 0.055	
			# of BLQ/ALQ Values	1/0	48/0	
		Vehicles	N	2	63	0.8186
			MEAN, GEO MEAN	0.005, NA	0.008, NA	
			SD, SE	0.0071, 0.0050	0.0177, 0.0022	
			MEDIAN	0.005	0.000	
			MIN, MAX	0.000, 0.010	0.000, 0.075	
			5%, 95%	0.000, 0.010	0.000, 0.055	
			# of BLQ/ALQ Values	1/0	48/0	
		Other places	N	21	44	0.0245
			MEAN, GEO MEAN	0.012, NA	0.007, NA	
			SD, SE	0.0194, 0.0042	0.0165, 0.0025	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.000, 0.075	0.000, 0.066	
			5%, 95%	0.000, 0.049	0.000, 0.055	
			# of BLQ/ALQ Values	13/0	36/0	
		Away from home combined	N	25	40	0.0152
			MEAN, GEO MEAN	0.012, NA	0.006, NA	
			SD, SE	0.0187, 0.0037	0.0165, 0.0026	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.000, 0.075	0.000, 0.066	
			5%, 95%	0.000, 0.049	0.000, 0.060	
			# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0536
			MEAN, GEO MEAN	0.176, 0.173	0.110, NA	
			SD, SE	0.0403, 0.0285	0.3723, 0.0469	
			MEDIAN	0.176	0.033	
			MIN, MAX	0.147, 0.204	0.000, 2.938	
			5%, 95%	0.147, 0.204	0.016, 0.209	
			# of BLQ/ALQ Values	0/0	0/0	
		Others at home	N	4	61	0.3297
			MEAN, GEO MEAN	0.105, 0.069	0.113, NA	
			SD, SE	0.0995, 0.0498	0.3780, 0.0484	
			MEDIAN	0.079	0.033	
			MIN, MAX	0.017, 0.243	0.000, 2.938	
			5%, 95%	0.017, 0.243	0.016, 0.204	
			# of BLQ/ALQ Values	0/0	0/0	
		At home combined	N	6	59	0.0486
			MEAN, GEO MEAN	0.128, 0.094	0.111, NA	
			SD, SE	0.0872, 0.0356	0.3843, 0.0500	
			MEDIAN	0.127	0.033	
			MIN, MAX	0.017, 0.243	0.000, 2.938	
			5%, 95%	0.017, 0.243	0.016, 0.209	
			# of BLQ/ALQ Values	0/0	0/0	
		Work	N	1	64	NA
			MEAN, GEO MEAN	0.209, 0.209	0.111, NA	
			SD, SE	NA, NA	0.3693, 0.0462	
			MEDIAN	0.209	0.033	
			MIN, MAX	0.209, 0.209	0.000, 2.938	
			5%, 95%	NA, NA	0.016, 0.204	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Vehicles	N	3	62	0.2510
			MEAN, GEO MEAN	0.094, 0.076	0.113, NA	
			SD, SE	0.0723, 0.0417	0.3753, 0.0477	
			MEDIAN	0.076	0.033	
			MIN, MAX	0.033, 0.174	0.000, 2.938	
			5%, 95%	0.033, 0.174	0.016, 0.209	
			# of BLQ/ALQ Values	0/0	0/0	
		Other places	N	20	45	0.0021
			MEAN, GEO MEAN	0.245, 0.084	0.053, NA	
			SD, SE	0.6463, 0.1445	0.0594, 0.0089	
			MEDIAN	0.075	0.033	
			MIN, MAX	0.016, 2.938	0.000, 0.243	
			5%, 95%	0.022, 1.772	0.016, 0.204	
			# of BLQ/ALQ Values	0/0	0/0	
		Away from home combined	N	23	42	0.0002
			MEAN, GEO MEAN	0.231, 0.087	0.047, NA	
			SD, SE	0.6024, 0.1256	0.0529, 0.0082	
			MEDIAN	0.076	0.030	
			MIN, MAX	0.016, 2.938	0.000, 0.243	
			5%, 95%	0.027, 0.606	0.016, 0.186	
			# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.2104
			MEAN, GEO MEAN	0.015, 0.015	0.040, NA	
			SD, SE	0.0042, 0.0030	0.2234, 0.0281	
			MEDIAN	0.015	0.006	
			MIN, MAX	0.012, 0.018	0.000, 1.782	
			5%, 95%	0.012, 0.018	0.000, 0.025	
			# of BLQ/ALQ Values	1/0	53/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Nicotine (nmol/mg Creatinine)	Others at home	N	4	61	0.2515
			MEAN, GEO MEAN	0.014, 0.012	0.041, NA	
			SD, SE	0.0057, 0.0029	0.2270, 0.0291	
			MEDIAN	0.015	0.006	
			MIN, MAX	0.006, 0.018	0.000, 1.782	
			5%, 95%	0.006, 0.018	0.000, 0.025	
			# of BLQ/ALQ Values	3/0	51/0	
		At home combined	N	6	59	0.0870
			MEAN, GEO MEAN	0.014, 0.013	0.041, NA	
			SD, SE	0.0049, 0.0020	0.2309, 0.0301	
			MEDIAN	0.015	0.006	
			MIN, MAX	0.006, 0.018	0.000, 1.782	
			5%, 95%	0.006, 0.018	0.000, 0.049	
			# of BLQ/ALQ Values	4/0	50/0	
		Work	N	1	64	NA
			MEAN, GEO MEAN	0.012, 0.012	0.039, NA	
			SD, SE	NA, NA	0.2216, 0.0277	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.012, 0.012	0.000, 1.782	
			5%, 95%	NA, NA	0.000, 0.025	
			# of BLQ/ALQ Values	0/0	54/0	
		Vehicles	N	3	62	0.0425
			MEAN, GEO MEAN	0.026, 0.022	0.039, NA	
			SD, SE	0.0199, 0.0115	0.2252, 0.0286	
			MEDIAN	0.018	0.006	
			MIN, MAX	0.012, 0.049	0.000, 1.782	
			5%, 95%	0.012, 0.049	0.000, 0.025	
			# of BLQ/ALQ Values	1/0	53/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Nicotine (nmol/mg Creatinine)	Other places	N	20	45	0.1713
			MEAN, GEO MEAN	0.104, NA	0.010, NA	
			SD, SE	0.3954, 0.0884	0.0063, 0.0009	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.000, 1.782	0.000, 0.025	
			5%, 95%	0.003, 0.934	0.000, 0.025	
			# of BLQ/ALQ Values	13/0	41/0	
		Away from home combined	N	23	42	0.0550
			MEAN, GEO MEAN	0.092, NA	0.010, NA	
			SD, SE	0.3687, 0.0769	0.0064, 0.0010	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.000, 1.782	0.000, 0.025	
			5%, 95%	0.006, 0.086	0.000, 0.025	
			# of BLQ/ALQ Values	14/0	40/0	
	Harrogate Cotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0247
			MEAN, GEO MEAN	0.034, 0.033	0.016, NA	
			SD, SE	0.0085, 0.0060	0.0402, 0.0051	
			MEDIAN	0.034	0.011	
			MIN, MAX	0.028, 0.040	0.000, 0.323	
			5%, 95%	0.028, 0.040	0.000, 0.028	
			# of BLQ/ALQ Values	0/0	47/0	
		Others at home	N	4	61	0.2778
			MEAN, GEO MEAN	0.019, 0.015	0.017, NA	
			SD, SE	0.0150, 0.0075	0.0408, 0.0052	
			MEDIAN	0.014	0.011	
			MIN, MAX	0.006, 0.040	0.000, 0.323	
			5%, 95%	0.006, 0.040	0.000, 0.028	
			# of BLQ/ALQ Values	2/0	45/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Cotinine (nmol/mg Creatinine)	At home combined	N	6	59	0.0243
			MEAN, GEO MEAN	0.024, 0.019	0.016, NA	
			SD, SE	0.0146, 0.0060	0.0414, 0.0054	
			MEDIAN	0.023	0.006	
			MIN, MAX	0.006, 0.040	0.000, 0.323	
			5%, 95%	0.006, 0.040	0.000, 0.028	
			# of BLQ/ALQ Values	2/0	45/0	
		Work	N	1	64	NA
			MEAN, GEO MEAN	0.011, 0.011	0.017, NA	
			SD, SE	NA, NA	0.0400, 0.0050	
			MEDIAN	0.011	0.011	
			MIN, MAX	0.011, 0.011	0.000, 0.323	
			5%, 95%	NA, NA	0.000, 0.040	
			# of BLQ/ALQ Values	0/0	47/0	
		Vehicles	N	3	62	0.1283
			MEAN, GEO MEAN	0.017, 0.016	0.017, NA	
			SD, SE	0.0060, 0.0035	0.0406, 0.0052	
			MEDIAN	0.017	0.009	
			MIN, MAX	0.011, 0.023	0.000, 0.323	
			5%, 95%	0.011, 0.023	0.000, 0.040	
			# of BLQ/ALQ Values	1/0	46/0	
		Other places	N	20	45	0.0388
			MEAN, GEO MEAN	0.029, NA	0.011, NA	
			SD, SE	0.0697, 0.0156	0.0093, 0.0014	
			MEDIAN	0.011	0.006	
			MIN, MAX	0.000, 0.323	0.000, 0.040	
			5%, 95%	0.003, 0.182	0.000, 0.028	
			# of BLQ/ALQ Values	9/0	38/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 20 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Cotinine (nmol/mg Creatinine)	Away from home combined	N	23	42	0.0123
			MEAN, GEO MEAN	0.027, NA	0.011, NA	
			SD, SE	0.0650, 0.0136	0.0095, 0.0015	
			MEDIAN	0.011	0.006	
			MIN, MAX	0.000, 0.323	0.000, 0.040	
			5%, 95%	0.006, 0.040	0.000, 0.028	
			# of BLQ/ALQ Values	10/0	37/0	
	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0398
			MEAN, GEO MEAN	0.089, 0.088	0.031, NA	
			SD, SE	0.0148, 0.0105	0.0642, 0.0081	
			MEDIAN	0.089	0.010	
			MIN, MAX	0.078, 0.099	0.000, 0.411	
			5%, 95%	0.078, 0.099	0.005, 0.099	
			# of BLQ/ALQ Values	0/0	17/0	
		Others at home	N	4	61	0.4685
			MEAN, GEO MEAN	0.037, 0.021	0.032, NA	
			SD, SE	0.0425, 0.0213	0.0654, 0.0084	
			MEDIAN	0.021	0.010	
			MIN, MAX	0.005, 0.099	0.000, 0.411	
			5%, 95%	0.005, 0.099	0.005, 0.099	
			# of BLQ/ALQ Values	1/0	16/0	
		At home combined	N	6	59	0.0658
			MEAN, GEO MEAN	0.054, 0.034	0.030, NA	
			SD, SE	0.0430, 0.0176	0.0657, 0.0086	
			MEDIAN	0.052	0.010	
			MIN, MAX	0.005, 0.099	0.000, 0.411	
			5%, 95%	0.005, 0.099	0.005, 0.109	
			# of BLQ/ALQ Values	1/0	16/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Work	N MEAN, GEO MEAN SD, SE MEDIAN MIN, MAX 5%, 95% # of BLQ/ALQ Values	1 0.109, 0.109 NA, NA 0.109 0.109, 0.109 NA, NA 0/0	64 0.031, NA 0.0638, 0.0080 0.010 0.000, 0.411 0.005, 0.099 17/0	NA
		Vehicles	N MEAN, GEO MEAN SD, SE MEDIAN MIN, MAX 5%, 95% # of BLQ/ALQ Values	3 0.024, 0.017 0.0242, 0.0140 0.010 0.010, 0.052 0.010, 0.052 1/0	62 0.033, NA 0.0654, 0.0083 0.010 0.000, 0.411 0.005, 0.099 16/0	0.7374
		Other places	N MEAN, GEO MEAN SD, SE MEDIAN MIN, MAX 5%, 95% # of BLQ/ALQ Values	20 0.061, 0.027 0.1050, 0.0235 0.021 0.005, 0.411 0.008, 0.354 4/0	45 0.020, NA 0.0256, 0.0038 0.010 0.000, 0.109 0.005, 0.099 13/0	0.0056
		Away from home combined	N MEAN, GEO MEAN SD, SE MEDIAN MIN, MAX 5%, 95% # of BLQ/ALQ Values	23 0.061, 0.028 0.0988, 0.0206 0.021 0.005, 0.411 0.010, 0.297 5/0	42 0.017, NA 0.0217, 0.0034 0.010 0.000, 0.099 0.005, 0.062 12/0	0.0009

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Spouse at home	N	1	58	NA
			MEAN, GEO MEAN	0.035, 0.035	0.009, NA	
			SD, SE	NA, NA	0.0187, 0.0024	
			MEDIAN	0.035	0.001	
			MIN, MAX	0.035, 0.035	0.000, 0.105	
			5%, 95%	NA, NA	0.000, 0.053	
			# of BLQ/ALQ Values	0/0	17/0	
		Others at home	N	4	55	0.4888
			MEAN, GEO MEAN	0.013, NA	0.009, NA	
			SD, SE	0.0191, 0.0096	0.0189, 0.0026	
			MEDIAN	0.005	0.001	
			MIN, MAX	0.000, 0.041	0.000, 0.105	
			5%, 95%	0.000, 0.041	0.000, 0.053	
			# of BLQ/ALQ Values	1/0	16/0	
		At home combined	N	5	54	0.1872
			MEAN, GEO MEAN	0.017, NA	0.008, NA	
			SD, SE	0.0193, 0.0086	0.0188, 0.0026	
			MEDIAN	0.008	0.001	
			MIN, MAX	0.000, 0.041	0.000, 0.105	
			5%, 95%	0.000, 0.041	0.000, 0.053	
			# of BLQ/ALQ Values	1/0	16/0	
		Work	N	1	58	NA
			MEAN, GEO MEAN	0.029, 0.029	0.009, NA	
			SD, SE	NA, NA	0.0188, 0.0025	
			MEDIAN	0.029	0.001	
			MIN, MAX	0.029, 0.029	0.000, 0.105	
			5%, 95%	NA, NA	0.000, 0.053	
			# of BLQ/ALQ Values	0/0	17/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Vehicles	N	3	56	0.9719
			MEAN, GEO MEAN	0.018, NA	0.009, NA	
			SD, SE	0.0303, 0.0175	0.0183, 0.0024	
			MEDIAN	0.001	0.001	
			MIN, MAX	0.000, 0.053	0.000, 0.105	
			5%, 95%	0.000, 0.053	0.000, 0.041	
			# of BLQ/ALQ Values	1/0	16/0	
		Other places	N	18	41	0.1658
			MEAN, GEO MEAN	0.015, NA	0.007, NA	
			SD, SE	0.0283, 0.0067	0.0123, 0.0019	
			MEDIAN	0.004	0.001	
			MIN, MAX	0.000, 0.105	0.000, 0.053	
			5%, 95%	0.000, 0.105	0.000, 0.035	
			# of BLQ/ALQ Values	4/0	13/0	
		Away from home combined	N	21	38	0.0387
			MEAN, GEO MEAN	0.017, NA	0.005, NA	
			SD, SE	0.0278, 0.0061	0.0093, 0.0015	
			MEDIAN	0.004	0.001	
			MIN, MAX	0.000, 0.105	0.000, 0.041	
			5%, 95%	0.000, 0.072	0.000, 0.035	
			# of BLQ/ALQ Values	5/0	12/0	
	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	61	0.0109
			MEAN, GEO MEAN	0.004, 0.003	0.006, NA	
			SD, SE	0.0007, 0.0005	0.0346, 0.0044	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.003, 0.004	0.000, 0.270	
			5%, 95%	0.003, 0.004	0.000, 0.011	
			# of BLQ/ALQ Values	1/0	53/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 24 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Others at home	N	4	59	0.1180
			MEAN, GEO MEAN	0.005, NA	0.006, NA	
			SD, SE	0.0076, 0.0038	0.0351, 0.0046	
			MEDIAN	0.002	0.000	
			MIN, MAX	0.000, 0.016	0.000, 0.270	
			5%, 95%	0.000, 0.016	0.000, 0.011	
			# of BLQ/ALQ Values	3/0	51/0	
		At home combined	N	6	57	0.0046
			MEAN, GEO MEAN	0.004, NA	0.006, NA	
			SD, SE	0.0060, 0.0024	0.0358, 0.0047	
			MEDIAN	0.003	0.000	
			MIN, MAX	0.000, 0.016	0.000, 0.270	
			5%, 95%	0.000, 0.016	0.000, 0.011	
			# of BLQ/ALQ Values	4/0	50/0	
		Work	N	1	62	NA
			MEAN, GEO MEAN	0.005, 0.005	0.006, NA	
			SD, SE	NA, NA	0.0343, 0.0044	
			MEDIAN	0.005	0.000	
			MIN, MAX	0.005, 0.005	0.000, 0.270	
			5%, 95%	NA, NA	0.000, 0.011	
			# of BLQ/ALQ Values	0/0	54/0	
		Vehicles	N	2	61	0.3307
			MEAN, GEO MEAN	0.002, NA	0.006, NA	
			SD, SE	0.0028, 0.0020	0.0346, 0.0044	
			MEDIAN	0.002	0.000	
			MIN, MAX	0.000, 0.004	0.000, 0.270	
			5%, 95%	0.000, 0.004	0.000, 0.011	
			# of BLQ/ALQ Values	1/0	53/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Other places	N	18	45	0.0562
			MEAN, GEO MEAN	0.017, NA	0.001, NA	
			SD, SE	0.0633, 0.0149	0.0028, 0.0004	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.270	0.000, 0.016	
			5%, 95%	0.000, 0.270	0.000, 0.005	
			# of BLQ/ALQ Values	13/0	41/0	
		Away from home combined	N	21	42	0.0063
			MEAN, GEO MEAN	0.015, NA	0.001, NA	
			SD, SE	0.0585, 0.0128	0.0028, 0.0004	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.270	0.000, 0.016	
			5%, 95%	0.000, 0.017	0.000, 0.003	
			# of BLQ/ALQ Values	14/0	40/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	63	0.1750
			MEAN, GEO MEAN	0.014, 0.013	0.011, NA	
			SD, SE	0.0049, 0.0035	0.0273, 0.0034	
			MEDIAN	0.014	0.000	
			MIN, MAX	0.010, 0.017	0.000, 0.195	
			5%, 95%	0.010, 0.017	0.000, 0.043	
			# of BLQ/ALQ Values	0/0	47/0	
		Others at home	N	4	61	0.2109
			MEAN, GEO MEAN	0.021, NA	0.010, NA	
			SD, SE	0.0241, 0.0120	0.0271, 0.0035	
			MEDIAN	0.020	0.000	
			MIN, MAX	0.000, 0.045	0.000, 0.195	
			5%, 95%	0.000, 0.045	0.000, 0.038	
			# of BLQ/ALQ Values	2/0	45/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 26 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	At home combined	N	6	59	0.0629
			MEAN, GEO MEAN	0.019, NA	0.010, NA	
			SD, SE	0.0192, 0.0078	0.0275, 0.0036	
			MEDIAN	0.014	0.000	
			MIN, MAX	0.000, 0.045	0.000, 0.195	
			5%, 95%	0.000, 0.045	0.000, 0.043	
			# of BLQ/ALQ Values	2/0	45/0	
		Work	N	1	64	NA
			MEAN, GEO MEAN	0.043, 0.043	0.010, NA	
			SD, SE	NA, NA	0.0268, 0.0033	
			MEDIAN	0.043	0.001	
			MIN, MAX	0.043, 0.043	0.000, 0.195	
			5%, 95%	NA, NA	0.000, 0.039	
			# of BLQ/ALQ Values	0/0	47/0	
		Vehicles	N	3	62	0.6528
			MEAN, GEO MEAN	0.008, NA	0.011, NA	
			SD, SE	0.0100, 0.0058	0.0274, 0.0035	
			MEDIAN	0.004	0.001	
			MIN, MAX	0.000, 0.019	0.000, 0.195	
			5%, 95%	0.000, 0.019	0.000, 0.043	
			# of BLQ/ALQ Values	1/0	46/0	
		Other places	N	20	45	0.0010
			MEAN, GEO MEAN	0.022, NA	0.006, NA	
			SD, SE	0.0425, 0.0095	0.0140, 0.0021	
			MEDIAN	0.011	0.000	
			MIN, MAX	0.000, 0.195	0.000, 0.058	
			5%, 95%	0.000, 0.117	0.000, 0.043	
			# of BLQ/ALQ Values	9/0	38/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 2	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Away from home combined	N	23	42	0.0003
			MEAN, GEO MEAN	0.021, NA	0.005, NA	
			SD, SE	0.0400, 0.0083	0.0131, 0.0020	
			MEDIAN	0.013	0.000	
			MIN, MAX	0.000, 0.195	0.000, 0.058	
			5%, 95%	0.000, 0.043	0.000, 0.039	
			# of BLQ/ALQ Values	10/0	37/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0199
			MEAN, GEO MEAN	0.322, 0.286	0.049, 0.036	
			SD, SE	0.2093, 0.1480	0.0500, 0.0063	
			MEDIAN	0.322	0.033	
			MIN, MAX	0.174, 0.470	0.011, 0.283	
			5%, 95%	0.174, 0.470	0.017, 0.109	
			# of BLQ/ALQ Values	0/0	0/0	
		Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.094, 0.094	0.056, 0.038	
			SD, SE	NA, NA	0.0738, 0.0092	
			MEDIAN	0.094	0.033	
			MIN, MAX	0.094, 0.094	0.011, 0.470	
			5%, 95%	NA, NA	0.017, 0.174	
			# of BLQ/ALQ Values	0/0	0/0	
		At home combined	N	3	62	0.0068
			MEAN, GEO MEAN	0.246, 0.197	0.048, 0.036	
			SD, SE	0.1981, 0.1144	0.0501, 0.0064	
			MEDIAN	0.174	0.033	
			MIN, MAX	0.094, 0.470	0.011, 0.283	
			5%, 95%	0.094, 0.470	0.017, 0.109	
			# of BLQ/ALQ Values	0/0	0/0	
		Work	N	5	60	0.2782
			MEAN, GEO MEAN	0.064, 0.053	0.056, 0.038	
			SD, SE	0.0367, 0.0164	0.0757, 0.0098	
			MEDIAN	0.051	0.033	
			MIN, MAX	0.016, 0.109	0.011, 0.470	
			5%, 95%	0.016, 0.109	0.017, 0.224	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

PM3006438810

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 29 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Vehicles	N	1	64	NA
			MEAN, GEO MEAN	0.470, 0.470	0.050, 0.037	
			SD, SE	NA, NA	0.0521, 0.0065	
			MEDIAN	0.470	0.033	
			MIN, MAX	0.470, 0.470	0.011, 0.283	
			5%, 95%	NA, NA	0.017, 0.139	
			# of BLQ/ALQ Values	0/0	0/0	
		Other places	N	10	33	0.1408
			MEAN, GEO MEAN	0.082, 0.056	0.052, 0.036	
			SD, SE	0.0811, 0.0256	0.0717, 0.0097	
			MEDIAN	0.062	0.033	
			MIN, MAX	0.017, 0.283	0.011, 0.470	
			5%, 95%	0.017, 0.283	0.017, 0.174	
			# of BLQ/ALQ Values	0/0	0/0	
		Away from home combined	N	15	50	0.0420
			MEAN, GEO MEAN	0.100, 0.061	0.044, 0.034	
			SD, SE	0.1228, 0.0317	0.0444, 0.0063	
			MEDIAN	0.054	0.033	
			MIN, MAX	0.016, 0.470	0.011, 0.274	
			5%, 95%	0.016, 0.470	0.017, 0.107	
			# of BLQ/ALQ Values	0/0	0/0	
	Harrogate Nicotine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0204
			MEAN, GEO MEAN	0.034, 0.030	0.010, NA	
			SD, SE	0.0219, 0.0155	0.0059, 0.0007	
			MEDIAN	0.034	0.006	
			MIN, MAX	0.018, 0.049	0.000, 0.031	
			5%, 95%	0.018, 0.049	0.000, 0.018	
			# of BLQ/ALQ Values	0/0	57/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 30 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Nicotine (nmol/mg Creatinine)	Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.012, 0.012	0.010, NA	
			SD, SE	NA, NA	0.0077, 0.0010	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.012, 0.012	0.000, 0.049	
			5%, 95%	NA, NA	0.000, 0.025	
			# of BLQ/ALQ Values	1/0	56/0	
		At home combined	N	3	62	0.0218
			MEAN, GEO MEAN	0.026, 0.022	0.010, NA	
			SD, SE	0.0199, 0.0115	0.0059, 0.0008	
			MEDIAN	0.018	0.006	
			MIN, MAX	0.012, 0.049	0.000, 0.031	
			5%, 95%	0.012, 0.049	0.000, 0.018	
			# of BLQ/ALQ Values	1/0	56/0	
		Work	N	5	60	0.4444
			MEAN, GEO MEAN	0.011, NA	0.010, NA	
			SD, SE	0.0066, 0.0029	0.0078, 0.0010	
			MEDIAN	0.012	0.006	
			MIN, MAX	0.000, 0.018	0.000, 0.049	
			5%, 95%	0.000, 0.018	0.003, 0.025	
			# of BLQ/ALQ Values	3/0	54/0	
		Vehicles	N	1	64	NA
			MEAN, GEO MEAN	0.049, 0.049	0.010, NA	
			SD, SE	NA, NA	0.0059, 0.0007	
			MEDIAN	0.049	0.006	
			MIN, MAX	0.049, 0.049	0.000, 0.031	
			5%, 95%	NA, NA	0.000, 0.018	
			# of BLQ/ALQ Values	0/0	57/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 31 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Nicotine (nmol/mg Creatinine)	Other places	N	10	55	0.1216
			MEAN, GEO MEAN	0.007, NA	0.011, NA	
			SD, SE	0.0038, 0.0012	0.0080, 0.0011	
			MEDIAN	0.006	0.012	
			MIN, MAX	0.000, 0.012	0.000, 0.049	
			5%, 95%	0.000, 0.012	0.000, 0.025	
			# of BLQ/ALQ Values	9/0	48/0	
		Away from home combined	N	15	50	0.6227
			MEAN, GEO MEAN	0.011, NA	0.010, NA	
			SD, SE	0.0116, 0.0030	0.0061, 0.0009	
			MEDIAN	0.006	0.009	
			MIN, MAX	0.000, 0.049	0.000, 0.031	
			5%, 95%	0.000, 0.049	0.006, 0.025	
			# of BLQ/ALQ Values	11/0	46/0	
	Harrogate Cotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0146
			MEAN, GEO MEAN	0.054, 0.047	0.011, NA	
			SD, SE	0.0361, 0.0255	0.0090, 0.0011	
			MEDIAN	0.054	0.006	
			MIN, MAX	0.028, 0.079	0.000, 0.051	
			5%, 95%	0.028, 0.079	0.006, 0.023	
			# of BLQ/ALQ Values	0/0	50/0	
		Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.011, 0.011	0.012, NA	
			SD, SE	NA, NA	0.0125, 0.0016	
			MEDIAN	0.011	0.009	
			MIN, MAX	0.011, 0.011	0.000, 0.079	
			5%, 95%	NA, NA	0.006, 0.028	
			# of BLQ/ALQ Values	0/0	50/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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RSR

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Table 14.14.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 32 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Cotinine (nmol/mg Creatinine)	At home combined	N	3	62	0.0200
			MEAN, GEO MEAN	0.039, 0.029	0.011, NA	
			SD, SE	0.0354, 0.0204	0.0090, 0.0011	
			MEDIAN	0.028	0.006	
			MIN, MAX	0.011, 0.079	0.000, 0.051	
			5%, 95%	0.011, 0.079	0.006, 0.023	
			# of BLQ/ALQ Values	0/0	50/0	
		Work	N	5	60	0.8536
			MEAN, GEO MEAN	0.010, NA	0.012, NA	
			SD, SE	0.0073, 0.0033	0.0127, 0.0016	
			MEDIAN	0.011	0.009	
			MIN, MAX	0.000, 0.017	0.000, 0.079	
			5%, 95%	0.000, 0.017	0.006, 0.040	
			# of BLQ/ALQ Values	3/0	47/0	
		Vehicles	N	1	64	NA
			MEAN, GEO MEAN	0.079, 0.079	0.011, NA	
			SD, SE	NA, NA	0.0091, 0.0011	
			MEDIAN	0.079	0.009	
			MIN, MAX	0.079, 0.079	0.000, 0.051	
			5%, 95%	NA, NA	0.006, 0.028	
			# of BLQ/ALQ Values	0/0	50/0	
		Other places	N	10	55	0.7480
			MEAN, GEO MEAN	0.014, 0.010	0.012, NA	
			SD, SE	0.0138, 0.0044	0.0122, 0.0016	
			MEDIAN	0.009	0.011	
			MIN, MAX	0.006, 0.051	0.000, 0.079	
			5%, 95%	0.006, 0.051	0.006, 0.028	
			# of BLQ/ALQ Values	5/0	45/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 33 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Cotinine (nmol/mg Creatinine)	Away from home combined	N	15	50	0.4381
			MEAN, GEO MEAN	0.017, NA	0.011, NA	
			SD, SE	0.0209, 0.0054	0.0081, 0.0012	
			MEDIAN	0.011	0.009	
			MIN, MAX	0.000, 0.079	0.000, 0.051	
			5%, 95%	0.000, 0.079	0.006, 0.028	
			# of BLQ/ALQ Values	7/0	43/0	
	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0178
			MEAN, GEO MEAN	0.151, 0.137	0.018, 0.012	
			SD, SE	0.0884, 0.0625	0.0203, 0.0026	
			MEDIAN	0.151	0.010	
			MIN, MAX	0.088, 0.213	0.005, 0.114	
			5%, 95%	0.088, 0.213	0.005, 0.042	
			# of BLQ/ALQ Values	0/0	30/0	
		Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.026, 0.026	0.022, 0.013	
			SD, SE	NA, NA	0.0328, 0.0041	
			MEDIAN	0.026	0.010	
			MIN, MAX	0.026, 0.026	0.005, 0.213	
			5%, 95%	NA, NA	0.005, 0.088	
			# of BLQ/ALQ Values	0/0	30/0	
		At home combined	N	3	62	0.0104
			MEAN, GEO MEAN	0.109, 0.079	0.018, 0.012	
			SD, SE	0.0953, 0.0550	0.0205, 0.0026	
			MEDIAN	0.088	0.010	
			MIN, MAX	0.026, 0.213	0.005, 0.114	
			5%, 95%	0.026, 0.213	0.005, 0.042	
			# of BLQ/ALQ Values	0/0	30/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 34 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Work	N	5	60	0.5174
			MEAN, GEO MEAN	0.019, 0.015	0.022, 0.013	
			SD, SE	0.0125, 0.0056	0.0337, 0.0043	
			MEDIAN	0.016	0.010	
			MIN, MAX	0.005, 0.036	0.005, 0.213	
			5%, 95%	0.005, 0.036	0.005, 0.091	
			# of BLQ/ALQ Values	0/0	30/0	
		Vehicles	N	1	54	NA
			MEAN, GEO MEAN	0.213, 0.213	0.019, 0.012	
			SD, SE	NA, NA	0.0220, 0.0028	
			MEDIAN	0.213	0.010	
			MIN, MAX	0.213, 0.213	0.005, 0.114	
			5%, 95%	NA, NA	0.005, 0.073	
			# of BLQ/ALQ Values	0/0	30/0	
		Other places	N	10	55	0.0410
			MEAN, GEO MEAN	0.035, 0.023	0.019, 0.012	
			SD, SE	0.0346, 0.0109	0.0319, 0.0043	
			MEDIAN	0.024	0.010	
			MIN, MAX	0.005, 0.114	0.005, 0.213	
			5%, 95%	0.005, 0.114	0.005, 0.088	
			# of BLQ/ALQ Values	0/0	30/0	
		Away from home combined	N	15	50	0.0208
			MEAN, GEO MEAN	0.041, 0.022	0.016, 0.011	
			SD, SE	0.0560, 0.0145	0.0183, 0.0026	
			MEDIAN	0.021	0.010	
			MIN, MAX	0.005, 0.213	0.005, 0.094	
			5%, 95%	0.005, 0.213	0.005, 0.042	
			# of BLQ/ALQ Values	0/0	30/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 35 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	59	0.0172
			MEAN, GEO MEAN	0.035, 0.031	0.004, NA	
			SD, SE	0.0219, 0.0155	0.0082, 0.0011	
			MEDIAN	0.035	0.001	
			MIN, MAX	0.019, 0.050	0.000, 0.040	
			5%, 95%	0.019, 0.050	0.000, 0.030	
			# of BLQ/ALQ Values	0/0	30/0	
		Others at home	N	1	60	NA
			MEAN, GEO MEAN	0.012, 0.012	0.005, NA	
			SD, SE	NA, NA	0.0102, 0.0013	
			MEDIAN	0.012	0.001	
			MIN, MAX	0.012, 0.012	0.000, 0.050	
			5%, 95%	NA, NA	0.000, 0.032	
			# of BLQ/ALQ Values	0/0	30/0	
		At home combined	N	3	58	0.0052
			MEAN, GEO MEAN	0.027, 0.023	0.004, NA	
			SD, SE	0.0202, 0.0117	0.0082, 0.0011	
			MEDIAN	0.019	0.001	
			MIN, MAX	0.012, 0.050	0.000, 0.040	
			5%, 95%	0.012, 0.050	0.000, 0.030	
			# of BLQ/ALQ Values	0/0	30/0	
		Work	N	4	57	0.1555
			MEAN, GEO MEAN	0.006, 0.003	0.005, NA	
			SD, SE	0.0080, 0.0040	0.0103, 0.0014	
			MEDIAN	0.003	0.000	
			MIN, MAX	0.001, 0.018	0.000, 0.050	
			5%, 95%	0.001, 0.018	0.000, 0.034	
			# of BLQ/ALQ Values	0/0	30/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 36 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Hartogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Vehicles	N	I	60	NA
			MEAN, GEO MEAN	0.050, 0.050	0.004, NA	
			SD, SE	NA, NA	0.0083, 0.0011	
			MEDIAN	0.050	0.001	
			MIN, MAX	0.050, 0.050	0.000, 0.040	
			5%, 95%	NA, NA	0.000, 0.025	
			# of BLQ/ALQ Values	0/0	30/0	
		Other places	N	9	52	0.0022
			MEAN, GEO MEAN	0.012, NA	0.004, NA	
			SD, SE	0.0125, 0.0042	0.0092, 0.0013	
			MEDIAN	0.009	0.000	
			MIN, MAX	0.000, 0.034	0.000, 0.050	
			5%, 95%	0.000, 0.034	0.000, 0.019	
			# of BLQ/ALQ Values	0/0	30/0	
		Away from home combined	N	13	48	0.0003
			MEAN, GEO MEAN	0.013, NA	0.003, NA	
			SD, SE	0.0158, 0.0044	0.0067, 0.0010	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.000, 0.050	0.000, 0.040	
			5%, 95%	0.000, 0.050	0.000, 0.012	
			# of BLQ/ALQ Values	0/0	30/0	
	Hartogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0065
			MEAN, GEO MEAN	0.012, 0.006	0.001, NA	
			SD, SE	0.0134, 0.0095	0.0024, 0.0003	
			MEDIAN	0.012	0.000	
			MIN, MAX	0.002, 0.021	0.000, 0.011	
			5%, 95%	0.002, 0.021	0.000, 0.006	
			# of BLQ/ALQ Values	0/0	57/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 37 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.004, 0.004	0.001, NA	
			SD, SE	NA, NA	0.0034, 0.0004	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.004, 0.004	0.000, 0.021	
			5%, 95%	NA, NA	0.000, 0.008	
			# of BLQ/ALQ Values	1/0	56/0	
		At home combined	N	3	62	0.0009
			MEAN, GEO MEAN	0.009, 0.006	0.001, NA	
			SD, SE	0.0104, 0.0060	0.0024, 0.0003	
			MEDIAN	0.004	0.000	
			MIN, MAX	0.002, 0.021	0.000, 0.011	
			5%, 95%	0.002, 0.021	0.000, 0.006	
			# of BLQ/ALQ Values	1/0	56/0	
		Work	N	5	60	0.2113
			MEAN, GEO MEAN	0.003, NA	0.001, NA	
			SD, SE	0.0050, 0.0022	0.0033, 0.0004	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.011	0.000, 0.021	
			5%, 95%	0.000, 0.011	0.000, 0.007	
			# of BLQ/ALQ Values	3/0	54/0	
		Vehicles	N	1	64	NA
			MEAN, GEO MEAN	0.021, 0.021	0.001, NA	
			SD, SE	NA, NA	0.0024, 0.0003	
			MEDIAN	0.021	0.000	
			MIN, MAX	0.021, 0.021	0.000, 0.011	
			5%, 95%	NA, NA	0.000, 0.006	
			# of BLQ/ALQ Values	0/0	57/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a A way from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 38 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Other places	N	10	55	0.1390
			MEAN, GEO MEAN	0.002, NA	0.001, NA	
			SD, SE	0.0026, 0.0008	0.0036, 0.0005	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.006	0.000, 0.021	
			5%, 95%	0.000, 0.006	0.000, 0.008	
			# of BLQ/ALQ Values	9/0	48/0	
		Away from home combined	N	15	50	0.0036
			MEAN, GEO MEAN	0.004, NA	0.001, NA	
			SD, SE	0.0058, 0.0015	0.0017, 0.0002	
			MEDIAN	0.000	0.000	
			MIN, MAX	0.000, 0.021	0.000, 0.008	
			5%, 95%	0.000, 0.021	0.000, 0.004	
			# of BLQ/ALQ Values	11/0	46/0	
	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0298
			MEAN, GEO MEAN	0.034, 0.024	0.006, NA	
			SD, SE	0.0332, 0.0235	0.0131, 0.0016	
			MEDIAN	0.034	0.000	
			MIN, MAX	0.010, 0.057	0.000, 0.067	
			5%, 95%	0.010, 0.057	0.000, 0.028	
			# of BLQ/ALQ Values	0/0	50/0	
		Others at home	N	1	64	NA
			MEAN, GEO MEAN	0.027, 0.027	0.006, NA	
			SD, SE	NA, NA	0.0142, 0.0018	
			MEDIAN	0.027	0.000	
			MIN, MAX	0.027, 0.027	0.000, 0.067	
			5%, 95%	NA, NA	0.000, 0.035	
			# of BLQ/ALQ Values	0/0	50/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 39 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	At home combined	N	3	62	0.0057
			MEAN, GEO MEAN	0.031, 0.025	0.005, NA	
			SD, SE	0.0238, 0.0137	0.0129, 0.0016	
			MEDIAN	0.027	0.000	
			MIN, MAX	0.010, 0.057	0.000, 0.067	
			5%, 95%	0.010, 0.057	0.000, 0.028	
			# of BLQ/ALQ Values	0/0	50/0	
		Work	N	5	60	0.0341
			MEAN, GEO MEAN	0.014, NA	0.006, NA	
			SD, SE	0.0148, 0.0066	0.0143, 0.0018	
			MEDIAN	0.011	0.000	
			MIN, MAX	0.000, 0.035	0.000, 0.067	
			5%, 95%	0.000, 0.035	0.000, 0.043	
			# of BLQ/ALQ Values	3/0	47/0	
		Vehicles	N	1	64	NA
			MEAN, GEO MEAN	0.057, 0.057	0.006, NA	
			SD, SE	NA, NA	0.0130, 0.0016	
			MEDIAN	0.057	0.000	
			MIN, MAX	0.057, 0.057	0.000, 0.067	
			5%, 95%	NA, NA	0.000, 0.028	
			# of BLQ/ALQ Values	0/0	50/0	
		Other places	N	10	55	0.0076
			MEAN, GEO MEAN	0.016, NA	0.005, NA	
			SD, SE	0.0210, 0.0067	0.0123, 0.0017	
			MEDIAN	0.010	0.000	
			MIN, MAX	0.000, 0.067	0.000, 0.060	
			5%, 95%	0.000, 0.067	0.000, 0.028	
			# of BLQ/ALQ Values	5/0	45/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 40 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 3	Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Away from home combined	N	15	50	0.0003
			MEAN, GEO MEAN	0.017, NA	0.003, NA	
			SD, SE	0.0210, 0.0054	0.0101, 0.0014	
			MEDIAN	0.011	0.000	
			MIN, MAX	0.000, 0.067	0.000, 0.060	
			5%, 95%	0.000, 0.067	0.000, 0.027	
			# of BLQ/ALQ Values	7/0	43/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 41 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 6	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Spouse at home	N	2	63	0.0551
			MEAN, GEO MEAN	14.12, 13.91	8.64, 7.82	
			SD, SE	3.373, 2.385	4.510, 0.568	
			MEDIAN	14.12	7.37	
			MIN, MAX	11.73, 16.50	4.09, 27.86	
			5%, 95%	11.73, 16.50	4.36, 15.91	
			# of BLQ/ALQ Values	0/0	0/0	
		Others at home	N	1	64	NA
			MEAN, GEO MEAN	9.65, 9.65	8.80, 7.94	
			SD, SE	NA, NA	4.594, 0.574	
			MEDIAN	9.65	7.44	
			MIN, MAX	9.65, 9.65	4.09, 27.86	
			5%, 95%	NA, NA	4.36, 16.50	
			# of BLQ/ALQ Values	0/0	0/0	
		At home combined	N	3	62	0.0406
			MEAN, GEO MEAN	12.63, 12.32	8.62, 7.79	
			SD, SE	3.512, 2.028	4.545, 0.577	
			MEDIAN	11.73	7.36	
			MIN, MAX	9.65, 16.50	4.09, 27.86	
			5%, 95%	9.65, 16.50	4.36, 15.91	
			# of BLQ/ALQ Values	0/0	0/0	
		Work	N	3	62	0.9129
			MEAN, GEO MEAN	8.01, 7.57	8.85, 7.98	
			SD, SE	3.360, 1.940	4.627, 0.588	
			MEDIAN	7.12	7.52	
			MIN, MAX	5.19, 11.73	4.09, 27.86	
			5%, 95%	5.19, 11.73	4.36, 16.50	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-3
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
(Page 42 of 42)

Timepoint	Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Week 6	Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Vehicles	N	3	62	0.2949
			MEAN, GEO MEAN	9.47, 9.30	8.78, 7.90	
			SD, SE	2.184, 1.261	4.651, 0.591	
			MEDIAN	9.31	7.43	
			MIN, MAX	7.37, 11.73	4.09, 27.86	
			5%, 95%	7.37, 11.73	4.36, 16.50	
			# of BLQ/ALQ Values	0/0	0/0	
		Other places	N	19	46	1.0000
			MEAN, GEO MEAN	9.30, 8.12	8.61, 7.89	
			SD, SE	6.063, 1.391	3.836, 0.566	
			MEDIAN	7.35	7.52	
			MIN, MAX	4.31, 27.86	4.09, 20.64	
			5%, 95%	4.31, 27.86	4.36, 15.91	
			# of BLQ/ALQ Values	0/0	0/0	
		Away from home combined	N	21	44	0.9497
			MEAN, GEO MEAN	9.10, 8.03	8.67, 7.93	
			SD, SE	5.785, 1.262	3.913, 0.590	
			MEDIAN	7.35	7.62	
			MIN, MAX	4.31, 27.86	4.09, 20.64	
			5%, 95%	4.49, 22.67	4.36, 15.91	
			# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 1 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Spouse at home	N	2	63	0.1656
		MEAN, GEO MEAN	9.17, 9.15	7.22, 6.44	
		SD, SE	0.856, 0.605	3.755, 0.473	
		MEDIAN	9.17	6.54	
		MIN, MAX	8.56, 9.77	2.49, 23.25	
		5%, 95%	8.56, 9.77	3.12, 13.59	
		# of BLQ/ALQ Values	0/0	0/0	
	Others at home	N	7	58	0.0865
		MEAN, GEO MEAN	8.98, 8.56	7.07, 6.30	
		SD, SE	3.036, 1.147	3.756, 0.493	
		MEDIAN	8.31	6.52	
		MIN, MAX	5.47, 13.87	2.49, 23.25	
		5%, 95%	5.47, 13.87	2.95, 13.59	
		# of BLQ/ALQ Values	0/0	0/0	
	At home combined	N	9	56	0.0250
		MEAN, GEO MEAN	9.02, 8.69	7.00, 6.22	
		SD, SE	2.648, 0.883	3.801, 0.508	
		MEDIAN	8.56	6.37	
		MIN, MAX	5.47, 13.87	2.49, 23.25	
		5%, 95%	5.47, 13.87	2.95, 13.59	
		# of BLQ/ALQ Values	0/0	0/0	
	Work	N	4	61	0.5391
		MEAN, GEO MEAN	8.05, 7.13	7.23, 6.48	
		SD, SE	3.839, 1.920	3.731, 0.478	
		MEDIAN	8.80	6.54	
		MIN, MAX	2.95, 11.63	2.49, 23.25	
		5%, 95%	2.95, 11.63	3.21, 13.59	
		# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 2 of 16)

Analytical Lab Biomarker	Source of Exposure*	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Vehicles	N	4	61	0.1947
		MEAN, GEO MEAN	8.80, 8.48	7.18, 6.40	
		SD, SE	2.600, 1.300	3.768, 0.482	
		MEDIAN	9.04	6.54	
		MIN, MAX	5.47, 11.63	2.49, 23.25	
		5%, 95%	5.47, 11.63	3.12, 13.59	
		# of BLQ/ALQ Values	0/0	0/0	
	Other places	N	21	44	0.4787
		MEAN, GEO MEAN	7.59, 6.86	7.13, 6.35	
		SD, SE	3.461, 0.755	3.857, 0.581	
		MEDIAN	6.95	6.54	
		MIN, MAX	2.95, 13.87	2.49, 23.25	
		5%, 95%	3.94, 13.59	3.12, 12.31	
		# of BLQ/ALQ Values	0/0	0/0	
	Away from home combined	N	25	40	0.2777
		MEAN, GEO MEAN	7.63, 6.98	7.06, 6.24	
		SD, SE	3.239, 0.648	4.004, 0.633	
		MEDIAN	7.34	6.52	
		MIN, MAX	2.95, 13.87	2.49, 23.25	
		5%, 95%	3.94, 13.59	3.01, 14.84	
		# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

* Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 3 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0331
		MEAN, GEO MEAN	0.308, 0.275	0.065, NA	
		SD, SE	0.1966, 0.1390	0.1100, 0.0139	
		MEDIAN	0.308	0.033	
		MIN, MAX	0.169, 0.447	0.000, 0.677	
		5%, 95%	0.169, 0.447	0.017, 0.306	
		# of BLQ/ALQ Values	0/0	0/0	
	Others at home	N	7	58	0.0584
		MEAN, GEO MEAN	0.184, 0.087	0.059, NA	
		SD, SE	0.2444, 0.0924	0.0886, 0.0116	
		MEDIAN	0.051	0.033	
		MIN, MAX	0.017, 0.677	0.000, 0.447	
		5%, 95%	0.017, 0.677	0.016, 0.306	
		# of BLQ/ALQ Values	0/0	0/0	
	At home combined	N	9	56	0.0055
		MEAN, GEO MEAN	0.212, 0.112	0.051, NA	
		SD, SE	0.2293, 0.0764	0.0715, 0.0096	
		MEDIAN	0.127	0.033	
		MIN, MAX	0.017, 0.677	0.000, 0.430	
		5%, 95%	0.017, 0.677	0.016, 0.183	
		# of BLQ/ALQ Values	0/0	0/0	
	Work	N	4	61	0.8903
		MEAN, GEO MEAN	0.059, 0.043	0.074, NA	
		SD, SE	0.0534, 0.0267	0.1221, 0.0156	
		MEDIAN	0.041	0.033	
		MIN, MAX	0.016, 0.136	0.000, 0.677	
		5%, 95%	0.016, 0.136	0.017, 0.340	
		# of BLQ/ALQ Values	0/0	0/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		Non-Smokers	P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers		
Week 1	N	6			
	MEAN, GEO MEAN	595.8, 333.9			
	SD, SE	849.24, 346.70			
	MEDIAN	293.4			
	MIN, MAX	97.7, 2316.6			
Week 2	5%, 95%	97.7, 2316.6			
	# of BLQ/ALQ Values	0/0			
Week 3	N	6			
	MEAN, GEO MEAN	791.5, 494.5			
	SD, SE	749.41, 305.95			
	MEDIAN	510.7			
	MIN, MAX	128.2, 1924.1			
Overall ^b	5%, 95%	128.2, 1924.1			
	# of BLQ/ALQ Values	0/0			
Week 1	N	5			
	MEAN, GEO MEAN	557.2, 321.5			
	SD, SE	516.34, 230.92			
	MEDIAN	262.2			
	MIN, MAX	41.0, 1181.9			
Week 2	5%, 95%	41.0, 1181.9			
	# of BLQ/ALQ Values	0/0			
Week 3	N	6			
	MEAN, GEO MEAN	649.3, 419.5			
	SD, SE	628.04, 256.40			
	MEDIAN	430.3			
	MIN, MAX	89.0, 1760.6			
Overall ^c	5%, 95%	89.0, 1760.6			

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 5 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Nicotine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0271
		MEAN, GEO MEAN	0.043, 0.041	0.019, NA	
		SD, SE	0.0170, 0.0120	0.0463, 0.0058	
		MEDIAN	0.043	0.006	
		MIN, MAX	0.031, 0.055	0.000, 0.271	
		5%, 95%	0.031, 0.055	0.000, 0.074	
		# of BLQ/ALQ Values	0/0	51/0	
	Others at home	N	7	58	0.0761
		MEAN, GEO MEAN	0.056, 0.021	0.015, NA	
		SD, SE	0.0913, 0.0345	0.0361, 0.0047	
		MEDIAN	0.012	0.006	
		MIN, MAX	0.006, 0.253	0.000, 0.271	
		5%, 95%	0.006, 0.253	0.000, 0.055	
		# of BLQ/ALQ Values	4/0	47/0	
	At home combined	N	9	56	0.0068
		MEAN, GEO MEAN	0.053, 0.025	0.014, NA	
		SD, SE	0.0795, 0.0265	0.0363, 0.0048	
		MEDIAN	0.018	0.006	
		MIN, MAX	0.006, 0.253	0.000, 0.271	
		5%, 95%	0.006, 0.253	0.000, 0.018	
		# of BLQ/ALQ Values	4/0	47/0	
	Work	N	4	61	0.1707
		MEAN, GEO MEAN	0.006, NA	0.021, NA	
		SD, SE	0.0049, 0.0024	0.0472, 0.0060	
		MEDIAN	0.006	0.012	
		MIN, MAX	0.000, 0.012	0.000, 0.271	
		5%, 95%	0.000, 0.012	0.006, 0.074	
		# of BLQ/ALQ Values	3/0	48/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 6 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Nicotine (nmol/mg Creatinine)	Vehicles	N	4	61	0.0491
		MEAN, GEO MEAN	0.041, 0.027	0.018, NA	
		SD, SE	0.0364, 0.0182	0.0463, 0.0059	
		MEDIAN	0.037	0.006	
		MIN, MAX	0.006, 0.086	0.000, 0.271	
		5%, 95%	0.006, 0.086	0.000, 0.031	
		# of BLQ/ALQ Values	2/0	49/0	
	Other places	N	21	44	0.8106
		MEAN, GEO MEAN	0.026, NA	0.017, NA	
		SD, SE	0.0589, 0.0128	0.0386, 0.0058	
		MEDIAN	0.006	0.012	
		MIN, MAX	0.000, 0.271	0.000, 0.253	
		5%, 95%	0.006, 0.074	0.000, 0.031	
		# of BLQ/ALQ Values	14/0	37/0	
	Away from home combined	N	25	40	0.9254
		MEAN, GEO MEAN	0.026, NA	0.016, NA	
		SD, SE	0.0555, 0.0111	0.0389, 0.0061	
		MEDIAN	0.006	0.012	
		MIN, MAX	0.000, 0.271	0.000, 0.253	
		5%, 95%	0.000, 0.086	0.003, 0.025	
		# of BLQ/ALQ Values	16/0	35/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 7 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Cotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0308
		MEAN, GEO MEAN	0.034, 0.032	0.013, NA	
		SD, SE	0.0156, 0.0110	0.0170, 0.0021	
		MEDIAN	0.034	0.006	
		MIN, MAX	0.023, 0.045	0.000, 0.114	
		5%, 95%	0.023, 0.045	0.000, 0.051	
		# of BLQ/ALQ Values	0/0	49/0	
	Others at home	N	7	58	0.0853
		MEAN, GEO MEAN	0.032, 0.017	0.011, NA	
		SD, SE	0.0404, 0.0153	0.0108, 0.0014	
		MEDIAN	0.011	0.006	
		MIN, MAX	0.006, 0.114	0.000, 0.057	
		5%, 95%	0.006, 0.114	0.000, 0.045	
		# of BLQ/ALQ Values	4/0	45/0	
	At home combined	N	9	56	0.0084
		MEAN, GEO MEAN	0.032, 0.020	0.010, NA	
		SD, SE	0.0355, 0.0118	0.0098, 0.0013	
		MEDIAN	0.017	0.006	
		MIN, MAX	0.006, 0.114	0.000, 0.057	
		5%, 95%	0.006, 0.114	0.000, 0.028	
		# of BLQ/ALQ Values	4/0	45/0	
	Work	N	4	61	0.7387
		MEAN, GEO MEAN	0.009, NA	0.014, NA	
		SD, SE	0.0072, 0.0036	0.0177, 0.0023	
		MEDIAN	0.009	0.006	
		MIN, MAX	0.000, 0.017	0.000, 0.114	
		5%, 95%	0.000, 0.017	0.006, 0.051	
		# of BLQ/ALQ Values	3/0	46/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Cotinine (nmol/mg Creatinine)	Vehicles	N	4	61	0.0537
		MEAN, GEO MEAN	0.031, 0.023	0.012, NA	
		SD, SE	0.0238, 0.0119	0.0164, 0.0021	
		MEDIAN	0.031	0.006	
		MIN, MAX	0.006, 0.057	0.000, 0.114	
		5%, 95%	0.006, 0.057	0.000, 0.028	
		# of BLQ/ALQ Values	2/0	47/0	
	Other places	N	21	44	0.4742
		MEAN, GEO MEAN	0.014, NA	0.013, NA	
		SD, SE	0.0161, 0.0035	0.0180, 0.0027	
		MEDIAN	0.006	0.011	
		MIN, MAX	0.000, 0.057	0.000, 0.114	
		5%, 95%	0.006, 0.051	0.000, 0.028	
		# of BLQ/ALQ Values	13/0	36/0	
	Away from home combined	N	25	40	0.9657
		MEAN, GEO MEAN	0.015, NA	0.012, NA	
		SD, SE	0.0173, 0.0035	0.0174, 0.0027	
		MEDIAN	0.006	0.011	
		MIN, MAX	0.000, 0.057	0.000, 0.114	
		5%, 95%	0.000, 0.057	0.003, 0.026	
		# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0228
		MEAN, GEO MEAN	0.149, 0.131	0.022, NA	
		SD, SE	0.0997, 0.0705	0.0338, 0.0043	
		MEDIAN	0.149	0.010	
		MIN, MAX	0.078, 0.219	0.000, 0.187	
		5%, 95%	0.078, 0.219	0.005, 0.083	
		# of BLQ/ALQ Values	0/0	22/0	
	Others at home	N	7	58	0.0993
		MEAN, GEO MEAN	0.063, 0.029	0.021, NA	
		SD, SE	0.0785, 0.0297	0.0335, 0.0044	
		MEDIAN	0.016	0.010	
		MIN, MAX	0.005, 0.187	0.000, 0.219	
		5%, 95%	0.005, 0.187	0.005, 0.083	
		# of BLQ/ALQ Values	2/0	20/0	
	At home combined	N	9	56	0.0086
		MEAN, GEO MEAN	0.082, 0.040	0.017, NA	
		SD, SE	0.0854, 0.0285	0.0192, 0.0026	
		MEDIAN	0.042	0.010	
		MIN, MAX	0.005, 0.219	0.000, 0.099	
		5%, 95%	0.005, 0.219	0.005, 0.068	
		# of BLQ/ALQ Values	2/0	20/0	
	Work	N	4	61	0.8557
		MEAN, GEO MEAN	0.023, 0.015	0.026, NA	
		SD, SE	0.0262, 0.0131	0.0428, 0.0055	
		MEDIAN	0.013	0.010	
		MIN, MAX	0.005, 0.062	0.000, 0.219	
		5%, 95%	0.005, 0.062	0.005, 0.099	
		# of BLQ/ALQ Values	1/0	21/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a A way from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Trans-3-hydroxycotinine (nmol/mg Creatinine)	Vehicles	N	4	61	0.0210
		MEAN, GEO MEAN	0.110, 0.057	0.020, NA	
		SD, SE	0.1088, 0.0544	0.0278, 0.0036	
		MEDIAN	0.102	0.010	
		MIN, MAX	0.016, 0.219	0.000, 0.166	
		5%, 95%	0.016, 0.219	0.005, 0.078	
		# of BLQ/ALQ Values	1/0	21/0	
	Other places	N	21	44	0.0481
		MEAN, GEO MEAN	0.034, 0.018	0.022, NA	
		SD, SE	0.0498, 0.0109	0.0374, 0.0056	
		MEDIAN	0.016	0.010	
		MIN, MAX	0.005, 0.219	0.000, 0.187	
		5%, 95%	0.005, 0.099	0.005, 0.078	
		# of BLQ/ALQ Values	3/0	19/0	
	Away from home combined	N	25	40	0.0126
		MEAN, GEO MEAN	0.039, 0.020	0.017, NA	
		SD, SE	0.0556, 0.0111	0.0277, 0.0044	
		MEDIAN	0.016	0.010	
		MIN, MAX	0.005, 0.219	0.000, 0.166	
		5%, 95%	0.005, 0.187	0.005, 0.060	
		# of BLQ/ALQ Values	4/0	18/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	51	0.0198
		MEAN, GEO MEAN	0.039, 0.036	0.005, NA	
		SD, SE	0.0198, 0.0140	0.0090, 0.0013	
		MEDIAN	0.039	0.001	
		MIN, MAX	0.025, 0.053	0.000, 0.051	
		5%, 95%	0.025, 0.053	0.000, 0.018	
		# of BLQ/ALQ Values	0/0	22/0	
	Others at home	N	7	46	0.5163
		MEAN, GEO MEAN	0.010, NA	0.006, NA	
		SD, SE	0.0184, 0.0069	0.0101, 0.0015	
		MEDIAN	0.003	0.001	
		MIN, MAX	0.000, 0.051	0.000, 0.053	
		5%, 95%	0.000, 0.051	0.000, 0.025	
		# of BLQ/ALQ Values	2/0	20/0	
	At home combined	N	9	44	0.0750
		MEAN, GEO MEAN	0.016, NA	0.004, NA	
		SD, SE	0.0216, 0.0072	0.0066, 0.0010	
		MEDIAN	0.005	0.001	
		MIN, MAX	0.000, 0.053	0.000, 0.034	
		5%, 95%	0.000, 0.053	0.000, 0.015	
		# of BLQ/ALQ Values	2/0	20/0	
	Work	N	4	49	0.7419
		MEAN, GEO MEAN	0.005, NA	0.006, NA	
		SD, SE	0.0048, 0.0024	0.0118, 0.0017	
		MEDIAN	0.004	0.002	
		MIN, MAX	0.000, 0.010	0.000, 0.053	
		5%, 95%	0.000, 0.010	0.000, 0.034	
		# of BLQ/ALQ Values	1/0	21/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Vehicles	N	4	49	0.3232
		MEAN, GEO MEAN	0.016, NA	0.005, NA	
		SD, SE	0.0230, 0.0125	0.0096, 0.0014	
		MEDIAN	0.005	0.001	
		MIN, MAX	0.000, 0.053	0.000, 0.051	
		5%, 95%	0.000, 0.053	0.000, 0.025	
		# of BLQ/ALQ Values	1/0	21/0	
	Other places	N	18	35	0.0016
		MEAN, GEO MEAN	0.010, NA	0.004, NA	
		SD, SE	0.0135, 0.0032	0.0097, 0.0016	
		MEDIAN	0.006	0.000	
		MIN, MAX	0.000, 0.053	0.000, 0.051	
		5%, 95%	0.000, 0.053	0.000, 0.025	
		# of BLQ/ALQ Values	3/0	19/0	
	Away from home combined	N	22	31	0.0021
		MEAN, GEO MEAN	0.009, NA	0.004, NA	
		SD, SE	0.0125, 0.0027	0.0103, 0.0018	
		MEDIAN	0.005	0.000	
		MIN, MAX	0.000, 0.053	0.000, 0.051	
		5%, 95%	0.000, 0.034	0.000, 0.025	
		# of BLQ/ALQ Values	4/0	18/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	60	0.3249
		MEAN, GEO MEAN	0.006, NA	0.002, NA	
		SD, SE	0.0085, 0.0060	0.0047, 0.0006	
		MEDIAN	0.006	0.000	
		MIN, MAX	0.000, 0.012	0.000, 0.023	
		5%, 95%	0.000, 0.012	0.000, 0.013	
		# of BLQ/ALQ Values	0/0	51/0	
	Others at home	N	6	56	0.0164
		MEAN, GEO MEAN	0.006, NA	0.002, NA	
		SD, SE	0.0080, 0.0033	0.0042, 0.0006	
		MEDIAN	0.003	0.000	
		MIN, MAX	0.000, 0.021	0.000, 0.023	
		5%, 95%	0.000, 0.021	0.000, 0.012	
		# of BLQ/ALQ Values	4/0	47/0	
	At home combined	N	8	54	0.0081
		MEAN, GEO MEAN	0.006, NA	0.001, NA	
		SD, SE	0.0075, 0.0026	0.0040, 0.0005	
		MEDIAN	0.003	0.000	
		MIN, MAX	0.000, 0.021	0.000, 0.023	
		5%, 95%	0.000, 0.021	0.000, 0.009	
		# of BLQ/ALQ Values	4/0	47/0	
	Work	N	4	58	0.3144
		MEAN, GEO MEAN	0.002, NA	0.002, NA	
		SD, SE	0.0024, 0.0012	0.0049, 0.0006	
		MEDIAN	0.002	0.000	
		MIN, MAX	0.000, 0.005	0.000, 0.023	
		5%, 95%	0.000, 0.005	0.000, 0.016	
		# of BLQ/ALQ Values	3/0	48/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Nicotine-N-glucuronide (nmol/mg Creatinine)	Vehicles	N	3	59	0.1050
		MEAN, GEO MEAN	0.005, NA	0.002, NA	
		SD, SE	0.0062, 0.0036	0.0047, 0.0006	
		MEDIAN	0.003	0.000	
		MIN, MAX	0.000, 0.012	0.000, 0.023	
		5%, 95%	0.000, 0.012	0.000, 0.016	
		# of BLQ/ALQ Values	2/0	49/0	
	Other places	N	20	42	0.0305
		MEAN, GEO MEAN	0.003, NA	0.001, NA	
		SD, SE	0.0057, 0.0013	0.0042, 0.0007	
		MEDIAN	0.000	0.000	
		MIN, MAX	0.000, 0.023	0.000, 0.021	
		5%, 95%	0.000, 0.018	0.000, 0.008	
		# of BLQ/ALQ Values	14/0	37/0	
	Away from home combined	N	23	39	0.0241
		MEAN, GEO MEAN	0.003, NA	0.001, NA	
		SD, SE	0.0054, 0.0011	0.0044, 0.0007	
		MEDIAN	0.000	0.000	
		MIN, MAX	0.000, 0.023	0.000, 0.021	
		5%, 95%	0.000, 0.012	0.000, 0.016	
		# of BLQ/ALQ Values	16/0	35/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Spouse at home	N	2	63	0.0334
		MEAN, GEO MEAN	0.038, 0.026	0.007, NA	
		SD, SE	0.0396, 0.0280	0.0161, 0.0020	
		MEDIAN	0.038	0.000	
		MIN, MAX	0.010, 0.066	0.000, 0.075	
		5%, 95%	0.010, 0.066	0.000, 0.049	
		# of BLQ/ALQ Values	0/0	49/0	
	Others at home	N	7	58	0.0736
		MEAN, GEO MEAN	0.022, NA	0.007, NA	
		SD, SE	0.0292, 0.0110	0.0150, 0.0020	
		MEDIAN	0.009	0.000	
		MIN, MAX	0.000, 0.075	0.000, 0.066	
		5%, 95%	0.000, 0.075	0.000, 0.055	
		# of BLQ/ALQ Values	4/0	45/0	
	At home combined	N	9	56	0.0074
		MEAN, GEO MEAN	0.026, NA	0.006, NA	
		SD, SE	0.0297, 0.0099	0.0130, 0.0017	
		MEDIAN	0.010	0.000	
		MIN, MAX	0.000, 0.075	0.000, 0.064	
		5%, 95%	0.000, 0.075	0.000, 0.036	
		# of BLQ/ALQ Values	4/0	45/0	
	Work	N	4	61	0.3227
		MEAN, GEO MEAN	0.011, NA	0.008, NA	
		SD, SE	0.0169, 0.0084	0.0176, 0.0023	
		MEDIAN	0.004	0.000	
		MIN, MAX	0.000, 0.036	0.000, 0.075	
		5%, 95%	0.000, 0.036	0.000, 0.055	
		# of BLQ/ALQ Values	3/0	46/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-4
Comparison Between Non-Smokers Exposed and Non-Smokers Not Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 16 of 16)

Analytical Lab Biomarker	Source of Exposure ^a	Statistic	Exposed	Not-exposed	P-value ^b
Harrogate Cotinine-N-glucuronide (nmol/mg Creatinine)	Vehicles	N	4	61	0.1024
		MEAN, GEO MEAN	0.024, NA	0.007, NA	
		SD, SE	0.0298, 0.0149	0.0162, 0.0021	
		MEDIAN	0.014	0.000	
		MIN, MAX	0.000, 0.066	0.000, 0.075	
		5%, 95%	0.000, 0.066	0.000, 0.049	
		# of BLQ/ALQ Values	2/0	47/0	
	Other places	N	21	44	0.0106
		MEAN, GEO MEAN	0.012, NA	0.006, NA	
		SD, SE	0.0196, 0.0043	0.0162, 0.0024	
		MEDIAN	0.006	0.000	
		MIN, MAX	0.000, 0.066	0.000, 0.075	
		5%, 95%	0.000, 0.064	0.000, 0.049	
		# of BLQ/ALQ Values	13/0	36/0	
	Away from home combined	N	25	40	0.0020
		MEAN, GEO MEAN	0.013, NA	0.006, NA	
		SD, SE	0.0189, 0.0038	0.0161, 0.0025	
		MEDIAN	0.006	0.000	
		MIN, MAX	0.000, 0.066	0.000, 0.075	
		5%, 95%	0.000, 0.064	0.000, 0.052	
		# of BLQ/ALQ Values	15/0	34/0	

NOTE: Source of exposure to environmental tobacco smoke is from at least one of the following: spouse at home, others at home, work, vehicles, other places.
Week 1 biomarker data used.

^a Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^b P-value from Wilcoxon rank-sum test.

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Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 1	4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.90, 0.86)	-0.09(0.8830)	0.00(1.0000)
			At home combined	(-0.76, 0.75)	-0.01(0.9909)	0.04(0.9365)
			Work	(-0.99, 0.73)	-0.77(0.2296)	-0.80(0.2000)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(-0.30, 0.54)	0.15(0.5220)	-0.06(0.8118)
			Away from home combined	(-0.33, 0.46)	0.08(0.7167)	-0.12(0.5542)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.90, 0.86)	-0.09(0.8830)	0.00(1.0000)
			At home combined	(-0.74, 0.76)	0.02(0.9633)	0.04(0.9365)
			Work	(-0.98, 0.93)	-0.31(0.6922)	-0.40(0.6000)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(-0.47, 0.39)	-0.04(0.8482)	-0.05(0.8447)
			Away from home combined	(-0.41, 0.38)	-0.02(0.9123)	-0.09(0.6573)
	Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.78)	-0.32(0.5948)	0.00(1.0000)
			At home combined	(-0.53, 0.88)	0.37(0.4181)	0.34(0.4601)
			Work	(-1.00, 0.14)	-0.95(0.0513)	-1.00(0.0000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.18, 0.63)	0.28(0.2233)	0.18(0.4361)
			Away from home combined	(-0.19, 0.57)	0.23(0.2792)	0.23(0.2724)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.78)	-0.32(0.5948)	0.00(1.0000)
			At home combined	(-0.50, 0.89)	0.40(0.3698)	0.34(0.4601)
			Work	(-1.00, 0.58)	-0.86(0.1376)	-0.80(0.2000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(0.01, 0.73)	0.44(0.0461)	0.20(0.3876)
			Away from home combined	(0.02, 0.69)	0.41(0.0411)	0.22(0.2969)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 1	Nicotine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.95, 0.74)	-0.41(0.4952)	-0.30(0.6186)
			At home combined	(-0.77, 0.73)	-0.05(0.9180)	0.25(0.5922)
			Work	(-0.94, 0.98)	0.23(0.7698)	0.21(0.7892)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(0.04, 0.75)	0.47(0.0331)	-0.07(0.7697)
			Away from home combined	(0.02, 0.69)	0.41(0.0421)	0.07(0.7532)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.95, 0.74)	-0.41(0.4952)	-0.30(0.6186)
			At home combined	(-0.75, 0.75)	0.00(0.9940)	0.25(0.5922)
			Work	(-0.78, 0.99)	0.72(0.2788)	0.74(0.2621)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(0.29, 0.84)	0.64(0.0018)	-0.04(0.8624)
			Away from home combined	(0.28, 0.81)	0.61(0.0012)	0.07(0.7294)
	Cotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.95, 0.74)	-0.41(0.4957)	-0.30(0.6186)
			At home combined	(-0.70, 0.80)	0.11(0.8179)	0.25(0.5922)
			Work	(-0.98, 0.94)	-0.22(0.7752)	-0.32(0.6838)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(-0.24, 0.59)	0.22(0.3489)	0.04(0.8746)
			Away from home combined	(-0.25, 0.52)	0.16(0.4463)	-0.04(0.8374)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.95, 0.74)	-0.41(0.4957)	-0.30(0.6186)
			At home combined	(-0.68, 0.81)	0.16(0.7377)	0.25(0.5922)
			Work	(-0.99, 0.88)	-0.51(0.4899)	-0.32(0.6838)
			Vehicles	(NA, NA)	1.00(NA)	1.00(NA)
			Other places	(-0.08, 0.69)	0.37(0.1025)	-0.03(0.8994)
			Away from home combined	(-0.08, 0.64)	0.33(0.1111)	-0.08(0.7045)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 1	Trans-3-hydroxycotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.93, 0.81)	-0.25(0.6802)	0.29(0.6376)
			At home combined	(-0.04, 0.96)	0.73(0.0609)	0.62(0.1395)
			Work	(-1.00, 0.54)	-0.87(0.1258)	-0.80(0.2000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.21, 0.61)	0.24(0.2871)	0.34(0.1261)
			Away from home combined	(-0.24, 0.53)	0.18(0.3990)	0.37(0.0676)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.93, 0.81)	-0.25(0.6802)	0.29(0.6376)
			At home combined	(-0.02, 0.96)	0.75(0.0545)	0.62(0.1395)
			Work	(-1.00, 0.02)	-0.96(0.0405)	-1.00(0.0000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.06, 0.70)	0.39(0.0842)	0.41(0.0618)
			Away from home combined	(-0.07, 0.55)	0.34(0.0984)	0.39(0.0556)
	Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.77)	-0.35(0.5629)	0.00(1.0000)
			At home combined	(-0.27, 0.93)	0.61(0.1472)	0.52(0.2274)
			Work	(-1.00, 0.56)	-0.87(0.1323)	-0.40(0.6000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.47, 0.44)	-0.01(0.9517)	0.23(0.3339)
			Away from home combined	(-0.45, 0.37)	-0.05(0.8360)	0.22(0.3070)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.77)	-0.35(0.5629)	0.00(1.0000)
			At home combined	(-0.24, 0.94)	0.62(0.1344)	0.52(0.2274)
			Work	(-1.00, 0.62)	-0.84(0.1563)	-0.80(0.2000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.38, 0.52)	0.08(0.7310)	0.38(0.1113)
			Away from home combined	(-0.35, 0.47)	0.07(0.7527)	0.31(0.1458)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 1	Nicotine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.78)	-0.33(0.5908)	-0.29(0.6376)
			At home combined	(-0.63, 0.84)	0.23(0.6177)	-0.14(0.7620)
			Work	(-0.99, 0.75)	-0.76(0.2450)	-0.80(0.2000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.50, 0.38)	-0.07(0.7550)	0.22(0.3524)
			Away from home combined	(-0.42, 0.39)	-0.02(0.9260)	0.32(0.1295)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.94, 0.78)	-0.33(0.5908)	-0.29(0.6376)
			At home combined	(-0.59, 0.86)	0.30(0.5168)	-0.14(0.7620)
			Work	(-0.98, 0.93)	-0.27(0.7295)	-0.40(0.6000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.32, 0.55)	0.15(0.5382)	0.41(0.0755)
			Away from home combined	(-0.20, 0.57)	0.22(0.3078)	0.42(0.0414)
	Cotinine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.89, 0.87)	-0.05(0.9378)	0.00(1.0000)
			At home combined	(-0.45, 0.90)	0.46(0.2997)	0.28(0.5420)
			Work	(-1.00, 0.31)	-0.93(0.0722)	-1.00(0.0000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.49, 0.36)	-0.08(0.7313)	0.39(0.0844)
			Away from home combined	(-0.48, 0.31)	-0.10(0.6330)	0.36(0.0755)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.89, 0.87)	-0.05(0.9378)	0.00(1.0000)
			At home combined	(-0.42, 0.91)	0.49(0.2661)	0.28(0.5420)
			Work	(-0.99, 0.74)	-0.76(0.2378)	-0.80(0.2000)
			Vehicles	(NA, NA)	-1.00(NA)	-1.00(NA)
			Other places	(-0.40, 0.46)	0.03(0.8843)	0.46(0.0355)
			Away from home combined	(-0.37, 0.42)	0.03(0.8896)	0.40(0.0468)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 2	Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(0.22, 1.00)	0.97(0.0251)	0.95(0.0513)
			At home combined	(-0.29, 0.96)	0.68(0.1371)	0.81(0.0499)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.22(0.8590)	0.00(1.0000)
			Other places	(-0.50, 0.38)	-0.08(0.7417)	0.47(0.0347)
			Away from home combined	(-0.46, 0.36)	-0.07(0.7672)	0.37(0.0807)
		Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(-0.24, 1.00)	0.94(0.0628)	0.95(0.0513)
			At home combined	(-0.76, 0.85)	0.14(0.7972)	0.81(0.0499)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.22(0.8590)	0.00(1.0000)
			Other places	(-0.47, 0.41)	-0.04(0.8798)	0.38(0.0939)
			Away from home combined	(-0.43, 0.40)	-0.02(0.9269)	0.22(0.3188)
	Nicotine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(-0.88, 0.99)	0.51(0.4863)	0.39(0.6111)
			At home combined	(-0.74, 0.87)	0.19(0.7242)	0.19(0.7215)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	-0.99(0.0965)	-0.87(0.3333)
			Other places	(-0.59, 0.26)	-0.21(0.3836)	-0.01(0.9562)
			Away from home combined	(-0.55, 0.25)	-0.18(0.4047)	0.01(0.9669)
		Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(-0.88, 0.99)	0.52(0.4780)	0.39(0.6111)
			At home combined	(-0.87, 0.74)	-0.18(0.7289)	0.19(0.7215)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	-0.99(0.0965)	-0.87(0.3333)
			Other places	(-0.57, 0.29)	-0.18(0.4605)	0.03(0.9120)
			Away from home combined	(-0.53, 0.28)	-0.15(0.5019)	0.01(0.9670)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 2	Cotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(-0.25, 1.00)	0.94(0.0642)	0.63(0.3675)
			At home combined	(-0.38, 0.95)	0.62(0.1871)	0.71(0.1170)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.00(1.0000)	0.00(1.0000)
			Other places	(-0.54, 0.33)	-0.13(0.5877)	0.31(0.1854)
			Away from home combined	(-0.50, 0.32)	-0.11(0.6171)	0.29(0.1782)
		Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(-0.09, 1.00)	0.95(0.0467)	0.63(0.3675)
			At home combined	(-0.74, 0.86)	0.17(0.7441)	0.71(0.1170)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.00(1.0000)	0.00(1.0000)
			Other places	(-0.51, 0.37)	-0.09(0.7138)	0.26(0.2608)
			Away from home combined	(-0.47, 0.36)	-0.07(0.7660)	0.22(0.3189)
	Trans-3-hydroxycotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(0.75, 1.00)	0.99(0.0036)	0.95(0.0313)
			At home combined	(-0.21, 0.97)	0.73(0.1026)	0.79(0.0592)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.50(0.6667)	0.50(0.6667)
			Other places	(-0.05, 0.71)	0.40(0.0826)	0.45(0.0440)
			Away from home combined	(-0.04, 0.69)	0.38(0.0718)	0.33(0.1216)
		Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(0.42, 1.00)	0.98(0.0161)	0.95(0.0313)
			At home combined	(-0.67, 0.89)	0.30(0.5607)	0.79(0.0592)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.50(0.6667)	0.50(0.6667)
			Other places	(0.04, 0.76)	0.47(0.0350)	0.42(0.0678)
			Away from home combined	(0.05, 0.73)	0.45(0.0293)	0.22(0.3034)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 2	Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	NA(NA)	NA(NA)
			Others at home	(0.95, 1.00)	1.00(0.0009)	0.95(0.0513)
			At home combined	(-0.15, 0.99)	0.84(0.0725)	0.97(0.0048)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.51(0.6562)	0.87(0.3333)
			Other places	(-0.11, 0.72)	0.38(0.1237)	0.23(0.3621)
			Away from home combined	(-0.15, 0.65)	0.30(0.1839)	0.12(0.5940)
		Weighted	Spouse at home	(NA, NA)	NA(NA)	NA(NA)
			Others at home	(0.55, 1.00)	0.99(0.0115)	0.95(0.0513)
			At home combined	(-0.28, 0.99)	0.80(0.1031)	0.97(0.0048)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.51(0.6562)	0.87(0.3333)
			Other places	(-0.02, 0.76)	0.45(0.0579)	0.22(0.3851)
			Away from home combined	(-0.07, 0.69)	0.37(0.0999)	0.03(0.9119)
	Nicotine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.96, 0.96)	0.03(0.9730)	0.78(0.2222)
			At home combined	(-0.81, 0.81)	0.00(0.9971)	0.63(0.1828)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.61, 0.30)	-0.20(0.4285)	0.22(0.3884)
			Away from home combined	(-0.56, 0.28)	-0.17(0.4597)	0.19(0.3995)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.97, 0.95)	-0.13(0.8749)	0.78(0.2222)
			At home combined	(-0.82, 0.80)	-0.03(0.9523)	0.63(0.1828)
			Work	(NA, NA)	NA(NA)	NA(NA)
		Weighted	Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.59, 0.33)	-0.17(0.5106)	0.20(0.4188)
			Away from home combined	(-0.54, 0.32)	-0.13(0.5610)	0.10(0.6706)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 2	Cotinine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.72, 1.00)	0.78(0.2181)	0.95(0.0513)
			At home combined	(-0.51, 0.94)	0.52(0.2951)	0.70(0.1248)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.32(0.7946)	0.00(1.0000)
			Other places	(-0.46, 0.42)	-0.02(0.9219)	0.54(0.0138)
			Away from home combined	(-0.43, 0.39)	-0.03(0.9083)	0.44(0.0342)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(-0.81, 0.99)	0.68(0.3219)	0.95(0.0513)
			At home combined	(-0.82, 0.81)	-0.02(0.9755)	0.70(0.1248)
			Work	(NA, NA)	NA(NA)	NA(NA)
			Vehicles	(NA, NA)	0.32(0.7946)	0.00(1.0000)
			Other places	(-0.45, 0.43)	-0.01(0.9666)	0.48(0.0337)
			Away from home combined	(-0.42, 0.40)	-0.01(0.9648)	0.31(0.1520)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 3	Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.98(0.1236)	1.00(0.0000)
			Work	(-0.60, 0.97)	0.60(0.2812)	0.37(0.5418)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.28, 0.83)	0.42(0.2247)	0.56(0.0910)
			Away from home combined	(0.35, 0.91)	0.73(0.0019)	0.57(0.0261)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.98(0.1296)	0.50(0.6667)
			Work	(-0.51, 0.98)	0.68(0.2076)	0.54(0.3467)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.48, 0.75)	0.22(0.5457)	0.53(0.1133)
			Away from home combined	(0.55, 0.94)	0.83(0.0001)	0.63(0.0111)
	Nicotine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.99(0.0906)	1.00(0.0000)
			Work	(-0.90, 0.86)	-0.08(0.8999)	-0.57(0.3120)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.67, 0.58)	-0.07(0.8410)	-0.09(0.8008)
			Away from home combined	(0.25, 0.88)	0.68(0.0056)	-0.02(0.9408)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.99(0.0966)	0.50(0.6667)
			Work	(-0.90, 0.87)	-0.07(0.9160)	-0.47(0.4228)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.82, 0.33)	-0.38(0.2747)	-0.44(0.2061)
			Away from home combined	(0.49, 0.93)	0.80(0.0003)	-0.05(0.8500)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 3	Cotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.97(0.1485)	1.00(0.0000)
			Work	(-0.90, 0.87)	-0.06(0.9197)	-0.29(0.6366)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.47, 0.75)	0.22(0.5343)	0.25(0.4824)
			Away from home combined	(0.18, 0.87)	0.64(0.0109)	0.29(0.2874)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.97(0.1545)	0.50(0.6667)
			Work	(-0.88, 0.88)	0.01(0.9874)	-0.11(0.8626)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.57, 0.68)	0.09(0.8062)	0.30(0.3960)
			Away from home combined	(0.41, 0.92)	0.76(0.0009)	0.38(0.1661)
	Trans-3-hydroxycotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.95(0.2051)	1.00(0.0000)
			Work	(-0.50, 0.98)	0.68(0.2036)	0.21(0.7406)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.19, 0.86)	0.50(0.1392)	0.61(0.0598)
			Away from home combined	(0.36, 0.91)	0.74(0.0017)	0.62(0.0140)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.95(0.2111)	0.50(0.6667)
			Work	(-0.50, 0.98)	0.68(0.2030)	0.32(0.6042)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.41, 0.78)	0.30(0.3982)	0.44(0.2036)
			Away from home combined	(0.58, 0.95)	0.84(0.0001)	0.62(0.0145)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b A way from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 3	Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.99(0.1048)	1.00(0.0000)
			Work	(0.62, 1.00)	0.99(0.0094)	0.80(0.2000)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(0.28, 0.95)	0.79(0.0105)	0.89(0.0015)
			Away from home combined	(0.38, 0.93)	0.77(0.0021)	0.93(0.0000)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.98(0.1108)	0.50(0.6667)
			Work	(0.17, 1.00)	0.97(0.0279)	0.63(0.3675)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.38, 0.83)	0.38(0.3097)	0.50(0.1747)
			Away from home combined	(0.42, 0.93)	0.79(0.0014)	0.81(0.0009)
	Nicotine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.99(0.0670)	0.50(0.6667)
			Work	(-0.95, 0.73)	-0.42(0.4794)	-0.34(0.5707)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.17, 0.86)	0.52(0.1274)	0.52(0.1232)
			Away from home combined	(0.05, 0.83)	0.55(0.0342)	0.24(0.3834)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	1.00(0.0610)	1.00(0.0000)
			Work	(-0.94, 0.79)	-0.31(0.6119)	-0.18(0.7761)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.08, 0.89)	0.58(0.0807)	0.56(0.0945)
			Away from home combined	(0.35, 0.90)	0.73(0.0020)	0.28(0.3122)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 3	Cotinine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.93(0.2384)	0.50(0.6667)
			Work	(-0.38, 0.98)	0.75(0.1403)	0.62(0.2690)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.36, 0.80)	0.35(0.3161)	0.56(0.0905)
			Away from home combined	(0.18, 0.87)	0.64(0.0109)	0.60(0.0180)
		Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	0.93(0.2324)	1.00(0.0000)
			Work	(-0.22, 0.99)	0.82(0.0877)	0.74(0.1546)
			Vehicles	(NA, NA)	NA(NA)	NA(NA)
			Other places	(-0.58, 0.68)	0.08(0.8278)	0.44(0.2036)
			Away from home combined	(0.14, 0.85)	0.61(0.0158)	0.60(0.0173)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-5
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Day Period Before Sample Collection
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Timepoint	Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Week 6	4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Non-Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	-0.18(0.8837)	0.50(0.6667)
			Work	(NA, NA)	0.82(0.3900)	1.00(0.0000)
			Vehicles	(NA, NA)	0.55(0.6263)	0.50(0.6667)
			Other places	(-0.62, 0.25)	-0.23(0.3532)	-0.23(0.3464)
			Away from home combined	(-0.52, 0.34)	-0.11(0.6312)	-0.17(0.4542)
		Weighted	Spouse at home	(NA, NA)	-1.00(NA)	-1.00(NA)
			Others at home	(NA, NA)	NA(NA)	NA(NA)
			At home combined	(NA, NA)	-0.22(0.8618)	0.50(0.6667)
			Work	(NA, NA)	0.52(0.6555)	0.50(0.6667)
			Vehicles	(NA, NA)	0.80(0.4140)	0.50(0.6667)
			Other places	(-0.60, 0.28)	-0.20(0.4090)	-0.14(0.5692)
			Away from home combined	(-0.48, 0.38)	-0.07(0.7762)	-0.11(0.6489)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-6
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.83, 0.64)	-0.21(0.6464)	0.21(0.6445)
		At home combined	(-0.71, 0.61)	-0.09(0.8150)	0.17(0.6682)
		Work	(-0.96, 0.96)	0.02(0.9847)	0.00(1.0000)
		Vehicles	(-0.94, 0.98)	0.25(0.7478)	0.32(0.6838)
		Other places	(-0.33, 0.52)	0.11(0.6232)	-0.03(0.9086)
		Away from home combined	(-0.29, 0.49)	0.12(0.5643)	-0.04(0.8463)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.83, 0.64)	-0.22(0.6397)	0.21(0.6445)
		At home combined	(-0.63, 0.70)	0.06(0.8807)	0.18(0.6368)
		Work	(-0.96, 0.96)	-0.04(0.9624)	0.00(1.0000)
		Vehicles	(-0.94, 0.98)	0.22(0.7781)	0.00(1.0000)
		Other places	(-0.42, 0.44)	0.01(0.9502)	-0.04(0.8531)
		Away from home combined	(-0.33, 0.46)	0.07(0.7234)	-0.08(0.7086)
Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.63, 0.84)	0.24(0.6093)	0.21(0.6445)
		At home combined	(-0.35, 0.84)	0.41(0.2708)	0.45(0.2242)
		Work	(-1.00, 0.62)	-0.84(0.1560)	-0.80(0.2000)
		Vehicles	(-0.80, 0.99)	0.70(0.3042)	0.32(0.6838)
		Other places	(-0.09, 0.68)	0.35(0.1146)	0.35(0.1230)
		Away from home combined	(-0.31, 0.47)	0.10(0.6495)	0.04(0.8403)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.53, 0.88)	0.37(0.4161)	0.21(0.6445)
		At home combined	(-0.31, 0.86)	0.45(0.2267)	0.50(0.1705)
		Work	(-1.00, 0.72)	-0.78(0.2162)	-0.80(0.2000)
		Vehicles	(-0.79, 0.99)	0.72(0.2848)	0.40(0.6000)
		Other places	(-0.06, 0.70)	0.38(0.0906)	0.25(0.2823)
		Away from home combined	(-0.33, 0.45)	0.07(0.7380)	-0.01(0.9576)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Table 14.1.4.2-6
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
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Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Nicotine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.69, 0.80)	0.13(0.7878)	0.16(0.7259)
		At home combined	(-0.62, 0.71)	0.08(0.8377)	0.40(0.2817)
		Work	(-0.99, 0.86)	-0.58(0.4159)	-0.63(0.3675)
		Vehicles	(-0.94, 0.97)	0.19(0.8088)	-0.32(0.6838)
		Other places	(0.02, 0.74)	0.44(0.0435)	0.49(0.0245)
		Away from home combined	(-0.37, 0.42)	0.03(0.8682)	0.18(0.3994)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.61, 0.85)	0.26(0.5707)	0.16(0.7259)
		At home combined	(-0.65, 0.70)	0.06(0.8707)	0.45(0.2198)
		Work	(-0.99, 0.78)	-0.72(0.2825)	-0.63(0.3675)
		Vehicles	(-0.94, 0.98)	0.22(0.7780)	-0.20(0.8000)
		Other places	(0.26, 0.83)	0.62(0.0028)	0.31(0.1673)
		Away from home combined	(-0.36, 0.43)	0.04(0.8461)	0.13(0.5397)
Cotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.63, 0.84)	0.23(0.6204)	0.16(0.7259)
		At home combined	(-0.50, 0.78)	0.24(0.5301)	0.40(0.2817)
		Work	(-1.00, -0.74)	-0.99(0.0060)	-1.00(0.0000)
		Vehicles	(-0.92, 0.98)	0.33(0.6715)	-0.32(0.6838)
		Other places	(-0.13, 0.66)	0.32(0.1517)	0.38(0.0871)
		Away from home combined	(-0.41, 0.38)	-0.02(0.9182)	0.00(0.9907)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.54, 0.88)	0.36(0.4253)	0.16(0.7259)
		At home combined	(-0.53, 0.77)	0.21(0.5913)	0.45(0.2198)
		Work	(-1.00, -0.44)	-0.98(0.0153)	-1.00(0.0000)
		Vehicles	(-0.92, 0.98)	0.36(0.6405)	-0.20(0.8000)
		Other places	(-0.02, 0.72)	0.41(0.0623)	0.25(0.2732)
		Away from home combined	(-0.42, 0.37)	-0.03(0.8803)	-0.02(0.9094)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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RSR

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Table 14.1.4.2-6
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 3 of 4)

Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Trans-3-hydroxycotinine (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.26, 0.93)	0.61(0.1431)	0.45(0.3104)
		At home combined	(0.21, 0.95)	0.77(0.0161)	0.67(0.0486)
		Work	(-1.00, 0.64)	-0.83(0.1680)	-0.80(0.2000)
		Vehicles	(-0.84, 0.99)	0.62(0.3766)	0.33(0.6667)
		Other places	(-0.26, 0.58)	0.19(0.4020)	0.20(0.3908)
		Away from home combined	(-0.33, 0.46)	0.08(0.7059)	-0.06(0.7915)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.09, 0.95)	0.71(0.0743)	0.45(0.3104)
		At home combined	(0.08, 0.93)	0.71(0.0332)	0.69(0.0412)
		Work	(-0.99, 0.76)	-0.75(0.2504)	-0.80(0.2000)
		Vehicles	(-0.83, 0.99)	0.64(0.3555)	0.32(0.6838)
		Other places	(-0.32, 0.54)	0.13(0.5607)	0.11(0.6399)
		Away from home combined	(-0.35, 0.44)	0.05(0.7990)	-0.10(0.6332)
Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.81, 0.68)	-0.15(0.7546)	0.25(0.5852)
		At home combined	(-0.38, 0.83)	0.38(0.3094)	0.49(0.1854)
		Work	(-0.99, 0.88)	-0.53(0.4744)	-0.40(0.6000)
		Vehicles	(0.66, 1.00)	0.99(0.0080)	0.63(0.3675)
		Other places	(-0.31, 0.60)	0.18(0.4725)	0.27(0.2871)
		Away from home combined	(-0.25, 0.57)	0.20(0.3826)	0.12(0.6054)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.76, 0.75)	-0.01(0.9803)	0.25(0.5852)
		At home combined	(-0.08, 0.91)	0.62(0.0755)	0.50(0.1684)
		Work	(-0.99, 0.87)	-0.55(0.4508)	-0.40(0.6000)
		Vehicles	(0.57, 1.00)	0.99(0.0108)	0.40(0.6000)
		Other places	(-0.45, 0.49)	0.02(0.9260)	0.19(0.4480)
		Away from home combined	(-0.32, 0.51)	0.12(0.6006)	0.04(0.8626)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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RSR

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Table 14.1.4.2-6
Comparison of Duration of Exposure of Non-Smokers Exposed to Environmental Tobacco Smoke by Source of Exposure Within 3-Month Period Before Sample Collection at Enrollment
(Page 4 of 4)

Biomarker	Duration of Exposure ^a	Independent Variable ^b	95% Confidence Interval ^c	Pearson Correlation Coefficient (P-value)	Spearman rank-order Coefficient (P-value)
Nicotine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.86, 0.75)	-0.15(0.7754)	0.12(0.8268)
		At home combined	(-0.62, 0.77)	0.15(0.7204)	0.15(0.7294)
		Work	(-0.99, 0.84)	-0.62(0.3785)	-0.63(0.3675)
		Vehicles	(NA, NA)	0.97(0.1544)	0.87(0.3333)
		Other places	(-0.28, 0.58)	0.19(0.4266)	0.20(0.3960)
		Away from home combined	(-0.35, 0.47)	0.08(0.7303)	0.12(0.5948)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.77, 0.85)	0.12(0.8200)	0.12(0.8268)
		At home combined	(-0.49, 0.84)	0.33(0.4194)	0.29(0.4816)
		Work	(-0.99, 0.84)	-0.64(0.3628)	-0.63(0.3675)
		Vehicles	(NA, NA)	0.96(0.1752)	0.50(0.6667)
		Other places	(-0.27, 0.59)	0.20(0.3989)	0.25(0.2946)
		Away from home combined	(-0.38, 0.44)	0.04(0.8583)	0.13(0.5518)
Cotinine-N-glucuronide (nmol/mg Creatinine)	Non-Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.79, 0.72)	-0.08(0.8631)	0.36(0.4271)
		At home combined	(-0.48, 0.79)	0.27(0.4890)	0.45(0.2220)
		Work	(-0.99, 0.74)	-0.76(0.2378)	-0.40(0.6000)
		Vehicles	(-0.30, 1.00)	0.93(0.0704)	0.32(0.6838)
		Other places	(-0.25, 0.58)	0.20(0.3882)	0.28(0.2151)
		Away from home combined	(-0.32, 0.46)	0.09(0.6858)	0.10(0.6317)
	Weighted	Spouse at home	(NA, NA)	1.00(NA)	1.00(NA)
		Others at home	(-0.74, 0.77)	0.04(0.9349)	0.36(0.4271)
		At home combined	(-0.24, 0.88)	0.50(0.1670)	0.52(0.1524)
		Work	(-0.99, 0.82)	-0.66(0.3402)	-0.40(0.6000)
		Vehicles	(-0.25, 1.00)	0.94(0.0638)	0.20(0.8090)
		Other places	(-0.37, 0.49)	0.07(0.7519)	0.24(0.2918)
		Away from home combined	(-0.36, 0.43)	0.04(0.8602)	0.07(0.7429)

^a Non-Weighted refers to the number of hours exposed to environmental tobacco smoke. For others at home, spouse at home, and at home combined, Weighted refers to the number of hours exposed to environmental tobacco smoke times the number of cigarettes smoked. For work, vehicles, other places, and away from home combined, weighted refers to the number of hours exposed to environmental tobacco smoke times the intensity (1=mild, 2=moderate, 3=severe) of smoke.

^b Away from home combined refers to exposure from at least one of the following: work, vehicles, other places. At home combined refers to at least one of the following: spouse at home, others at home.

^c 95% confidence interval for the correlation coefficient.

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Covance CRU Study No. 12226-8450

14.2 Statistical Comparison of Biomarkers of Exposure

14.2.1 Overall Comparison Between Smokers and Non-Smokers

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 14)

Biomarker: Acetonitrile (ng/mL)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	313.81, 219.47	178.65, 97.51	
	SD, SE	322.285, 45.578	287.366, 35.643	
	MEDIAN	201.20	90.66	
	MIN, MAX	51.48, 1500.00	30.00, 1500.00	
	5%, 95%	75.16, 1089.74	30.00, 812.94	
	# of BLQ/ALQ Values	1/1	16/1	
Week 2	N	48	65	0.0002
	MEAN, GEO MEAN	357.78, 245.18	179.27, 115.61	
	SD, SE	332.195, 47.948	176.528, 21.896	
	MEDIAN	247.22	104.08	
	MIN, MAX	30.00, 1500.00	30.00, 756.74	
	5%, 95%	54.06, 1002.96	30.00, 610.62	
	# of BLQ/ALQ Values	1/2	12/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	544.89, 343.31	206.46, 133.78	
	SD, SE	576.013, 84.929	219.008, 27.165	
	MEDIAN	311.35	126.23	
	MIN, MAX	46.59, 2000.00	30.00, 1168.91	
	5%, 95%	76.49, 2000.00	30.00, 619.94	
	# of BLQ/ALQ Values	0/5	10/0	
Week 6	N	42	65	0.0004
	MEAN, GEO MEAN	439.65, 287.66	224.64, 133.92	
	SD, SE	421.896, 65.100	232.664, 28.858	
	MEDIAN	284.89	119.94	
	MIN, MAX	31.68, 1500.00	30.00, 947.36	
	5%, 95%	97.44, 1406.38	30.00, 670.92	
	# of BLQ/ALQ Values	0/1	13/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	409.36, 326.55	197.26, 159.57	
	SD, SE	270.039, 38.189	135.413, 16.796	
	MEDIAN	352.45	156.31	
	MIN, MAX	82.80, 1084.24	30.00, 701.92	
	5%, 95%	86.83, 1006.07	44.47, 452.36	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 14)

Biomarker: Acetonitrile (nmol/L)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	7650.8, 5350.7	4355.5, 2377.2	
	SD, SE	7857.31, 1111.19	7005.98, 868.99	
	MEDIAN	4905.3	2210.3	
	MIN, MAX	1255.1, 36570.0	731.4, 36570.0	
	5%, 95%	1832.4, 26567.9	731.4, 19819.5	
	# of BLQ/ALQ Values	1/1	16/1	
Week 2	N	48	65	0.0002
	MEAN, GEO MEAN	8722.7, 5977.6	4370.5, 2818.5	
	SD, SE	8098.92, 1168.98	4303.74, 533.81	
	MEDIAN	6027.1	2537.5	
	MIN, MAX	731.4, 36570.0	731.4, 18449.3	
	5%, 95%	1318.0, 24452.2	731.4, 14886.9	
	# of BLQ/ALQ Values	1/2	12/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	13284.4, 8369.8	5033.4, 3261.6	
	SD, SE	14043.21, 2070.56	5339.41, 662.27	
	MEDIAN	7590.7	3077.5	
	MIN, MAX	1135.9, 48760.0	731.4, 28498.0	
	5%, 95%	1864.8, 48760.0	731.4, 15114.1	
	# of BLQ/ALQ Values	0/5	10/0	
Week 6	N	42	65	0.0004
	MEAN, GEO MEAN	10718.6, 7013.0	5476.8, 3265.0	
	SD, SE	10285.83, 1587.14	5672.36, 703.57	
	MEDIAN	6945.6	2924.1	
	MIN, MAX	772.4, 36570.0	731.4, 23096.6	
	5%, 95%	2375.6, 34287.5	731.4, 16357.0	
	# of BLQ/ALQ Values	0/1	13/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	9980.1, 7961.1	4809.1, 3890.3	
	SD, SE	6583.55, 931.05	3301.38, 409.49	
	MEDIAN	8592.6	3810.7	
	MIN, MAX	2018.6, 26433.8	731.4, 17112.8	
	5%, 95%	2116.9, 24527.9	1084.1, 11028.6	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 14)

Biomarker: Acetonitrile ((ng/mL)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	24.91, 16.86		
	SD, SE	25.207, 3.565		
	MEDIAN	14.34		
	MIN, MAX	3.39, 116.91		
	5%, 95%	5.47, 84.16		
	# of BLQ/ALQ Values	1/1		
Week 2	N	48		NA
	MEAN, GEO MEAN	32.28, 19.21		
	SD, SE	42.578, 6.146		
	MEDIAN	15.81		
	MIN, MAX	3.93, 205.14		
	5%, 95%	5.98, 150.00		
	# of BLQ/ALQ Values	1/2		
Week 3	N	46		NA
	MEAN, GEO MEAN	56.90, 27.36		
	SD, SE	81.200, 11.972		
	MEDIAN	21.09		
	MIN, MAX	4.25, 333.33		
	5%, 95%	7.09, 250.00		
	# of BLQ/ALQ Values	0/5		
Week 6	N	42		NA
	MEAN, GEO MEAN	47.33, 21.54		
	SD, SE	108.798, 16.788		
	MEDIAN	18.74		
	MIN, MAX	3.17, 703.19		
	5%, 95%	5.17, 127.61		
	# of BLQ/ALQ Values	0/1		
Overall [*]	N	50		NA
	MEAN, GEO MEAN	39.94, 26.59		
	SD, SE	45.691, 6.462		
	MEDIAN	28.87		
	MIN, MAX	4.35, 264.63		
	5%, 95%	7.46, 129.96		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 14)

Biomarker: Acetonitrile ((nmol/L)/cigarette per day)		Analytical Lab: Madison	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	607.2, 411.0	
	SD, SE	614.52, 86.91	
	MEDIAN	349.5	
	MIN, MAX	82.7, 2850.2	
	5%, 95%	133.3, 2051.9	
	# of BLQ/ALQ Values	1/1	
Week 2	N	48	
	MEAN, GEO MEAN	787.0, 468.2	
	SD, SE	1038.05, 149.83	
	MEDIAN	385.4	
	MIN, MAX	95.9, 5001.3	
	5%, 95%	145.7, 3657.0	
	# of BLQ/ALQ Values	1/2	
Week 3	N	46	
	MEAN, GEO MEAN	1387.2, 667.2	
	SD, SE	1979.68, 291.89	
	MEDIAN	514.0	
	MIN, MAX	103.6, 8126.7	
	5%, 95%	172.7, 6095.0	
	# of BLQ/ALQ Values	0/5	
Week 6	N	42	
	MEAN, GEO MEAN	1153.9, 525.1	
	SD, SE	2652.49, 409.29	
	MEDIAN	456.7	
	MIN, MAX	77.2, 17143.8	
	5%, 95%	126.1, 3111.1	
	# of BLQ/ALQ Values	0/1	
Overall*	N	50	
	MEAN, GEO MEAN	973.7, 648.3	
	SD, SE	1113.95, 157.54	
	MEDIAN	703.7	
	MIN, MAX	106.1, 6451.6	
	5%, 95%	181.7, 3168.4	
			NA

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 5 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	3.80, 2.70	0.59, 0.54	
	SD, SE	3.377, 0.482	0.511, 0.063	
	MEDIAN	2.58	0.50	
	MIN, MAX	0.50, 15.03	0.50, 4.59	
	5%, 95%	0.87, 10.43	0.50, 0.77	
	# of BLQ/ALQ Values	2/0	53/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	5.36, 2.93	0.59, 0.55	
	SD, SE	9.783, 1.510	0.336, 0.042	
	MEDIAN	3.11	0.50	
	MIN, MAX	0.50, 63.34	0.50, 2.46	
	5%, 95%	0.50, 12.65	0.50, 1.35	
	# of BLQ/ALQ Values	3/0	59/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	4.39, 2.89	0.59, 0.56	
	SD, SE	5.147, 0.728	0.303, 0.038	
	MEDIAN	2.79	0.50	
	MIN, MAX	0.50, 32.18	0.50, 2.55	
	5%, 95%	0.81, 13.14	0.50, 1.09	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
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Biomarker: 3-Aminobiphenyl-Hb adduct ((ng/g hemoglobin)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	0.27, 0.21		
	SD, SE	0.225, 0.032		
	MEDIAN	0.21		
	MIN, MAX	0.06, 1.17		
	5%, 95%	0.06, 0.57		
	# of BLQ/ALQ Values	2/0		
Week 6	N	42		NA
	MEAN, GEO MEAN	1.05, 0.22		
	SD, SE	4.858, 0.750		
	MEDIAN	0.18		
	MIN, MAX	0.03, 31.57		
	5%, 95%	0.05, 1.05		
	# of BLQ/ALQ Values	3/0		
Overall [*]	N	50		NA
	MEAN, GEO MEAN	0.60, 0.23		
	SD, SE	2.242, 0.317		
	MEDIAN	0.22		
	MIN, MAX	0.05, 16.01		
	5%, 95%	0.06, 1.11		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 7 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	34.39, 28.34	7.28, 6.51	
	SD, SE	21.781, 3.112	3.713, 0.460	
	MEDIAN	28.94	6.55	
	MIN, MAX	5.35, 100.50	2.49, 23.25	
	5%, 95%	8.56, 87.23	3.12, 13.59	
	# of BLQ/ALQ Values	0/0	0/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	59.01, 37.81	8.81, 7.96	
	SD, SE	120.309, 18.564	4.559, 0.566	
	MEDIAN	38.15	7.50	
	MIN, MAX	7.27, 808.80	4.09, 27.86	
	5%, 95%	9.56, 90.32	4.36, 16.50	
	# of BLQ/ALQ Values	0/0	0/0	
Overall [*]	N	50	65	<.0001
	MEAN, GEO MEAN	44.31, 33.14	8.05, 7.35	
	SD, SE	56.254, 7.956	3.826, 0.475	
	MEDIAN	34.25	7.02	
	MIN, MAX	6.31, 408.68	3.62, 22.96	
	5%, 95%	11.43, 82.02	3.88, 15.04	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct ((pg/g hemoglobin)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	2.79, 2.20		
	SD, SE	2.710, 0.387		
	MEDIAN	2.17		
	MIN, MAX	0.59, 18.14		
	5%, 95%	0.90, 6.43		
	# of BLQ/ALQ Values	0/0		
Week 6	N	42		NA
	MEAN, GEO MEAN	12.99, 2.83		
	SD, SE	62.106, 9.581		
	MEDIAN	2.38		
	MIN, MAX	0.95, 404.40		
	5%, 95%	1.29, 8.15		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	50		NA
	MEAN, GEO MEAN	7.07, 2.62		
	SD, SE	28.615, 4.047		
	MEDIAN	2.19		
	MIN, MAX	0.90, 203.63		
	5%, 95%	1.16, 8.27		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 9 of 14)

Biomarker: Carboxyhemoglobin (% saturation) Analytical Lab: CCLS				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	4.4, 3.3	0.4, 0.4	
	SD, SE	3.14, 0.44	0.17, 0.02	
	MEDIAN	4.0	0.3	
	MIN, MAX	0.3, 14.8	0.3, 1.0	
	5%, 95%	0.9, 11.3	0.3, 0.7	
	# of BLQ/ALQ Values	1/0	39/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	4.0, 2.8	0.4, 0.3	
	SD, SE	3.01, 0.43	0.16, 0.02	
	MEDIAN	3.4	0.3	
	MIN, MAX	0.3, 13.3	0.3, 1.1	
	5%, 95%	0.3, 9.8	0.3, 0.8	
	# of BLQ/ALQ Values	3/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	4.7, 3.6	0.5, 0.4	
	SD, SE	3.03, 0.45	0.50, 0.06	
	MEDIAN	4.0	0.3	
	MIN, MAX	0.3, 11.3	0.3, 2.8	
	5%, 95%	0.7, 10.4	0.3, 1.6	
	# of BLQ/ALQ Values	1/0	38/0	
Week 6	N	41	65	<.0001
	MEAN, GEO MEAN	4.7, 3.5	0.4, 0.4	
	SD, SE	2.96, 0.46	0.20, 0.03	
	MEDIAN	4.1	0.3	
	MIN, MAX	0.3, 13.9	0.3, 1.3	
	5%, 95%	0.4, 9.2	0.3, 0.8	
	# of BLQ/ALQ Values	2/0	34/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	4.4, 3.3	0.4, 0.4	
	SD, SE	2.90, 0.41	0.19, 0.02	
	MEDIAN	4.0	0.4	
	MIN, MAX	0.3, 12.2	0.3, 1.3	
	5%, 95%	0.7, 9.8	0.3, 0.8	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 10 of 14)

Biomarker: Carboxyhemoglobin ((% saturation)/cigarette per day)		Analytical Lab: CCLS		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	0.3, 0.3		
	SD, SE	0.42, 0.06		
	MEDIAN	0.2		
	MIN, MAX	0.1, 3.0		
	5%, 95%	0.1, 0.8		
	# of BLQ/ALQ Values	1/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.3, NA		
	SD, SE	0.60, 0.09		
	MEDIAN	0.2		
	MIN, MAX	0.0, 4.3		
	5%, 95%	0.1, 0.5		
	# of BLQ/ALQ Values	3/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.4, 0.3		
	SD, SE	0.35, 0.05		
	MEDIAN	0.3		
	MIN, MAX	0.1, 2.3		
	5%, 95%	0.1, 0.9		
	# of BLQ/ALQ Values	1/0		
Week 6	N	41		NA
	MEAN, GEO MEAN	0.5, 0.3		
	SD, SE	1.07, 0.17		
	MEDIAN	0.3		
	MIN, MAX	0.1, 7.0		
	5%, 95%	0.1, 0.7		
	# of BLQ/ALQ Values	2/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	0.4, 0.3		
	SD, SE	0.58, 0.08		
	MEDIAN	0.3		
	MIN, MAX	0.1, 4.2		
	5%, 95%	0.1, 0.7		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
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Biomarker: 3-Aminobiphenyl-Hb adduct (pg/g hemoglobin)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	3	8	0.6831
	MEAN, GEO MEAN	0.70, 0.70	1.44, 0.93	
	SD, SE	0.000, 0.000	2.082, 0.736	
	MEDIAN	0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 6.59	
	5%, 95%	0.70, 0.70	0.70, 6.59	
	# of BLQ/ALQ Values	3/0	7/0	
Week 6	N	3	8	1.0000
	MEAN, GEO MEAN	0.70, 0.70	0.70, 0.70	
	SD, SE	0.000, 0.000	0.000, 0.000	
	MEDIAN	0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 0.70	
	5%, 95%	0.70, 0.70	0.70, 0.70	
	# of BLQ/ALQ Values	3/0	8/0	
Overall [*]	N	5	8	0.5271
	MEAN, GEO MEAN	0.70, 0.70	1.07, 0.86	
	SD, SE	0.000, 0.000	1.043, 0.369	
	MEDIAN	0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 3.65	
	5%, 95%	0.70, 0.70	0.70, 3.65	

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 12 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct ((pg/g hemoglobin)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	3		NA
	MEAN, GEO MEAN	0.07, 0.07		
	SD, SE	0.042, 0.024		
	MEDIAN	0.06		
	MIN, MAX	0.04, 0.12		
	5%, 95%	0.04, 0.12		
	# of BLQ/ALQ Values	3/0		
Week 6	N	3		NA
	MEAN, GEO MEAN	0.10, 0.08		
	SD, SE	0.074, 0.043		
	MEDIAN	0.07		
	MIN, MAX	0.04, 0.18		
	5%, 95%	0.04, 0.18		
	# of BLQ/ALQ Values	3/0		
Overall*	N	5		NA
	MEAN, GEO MEAN	0.08, 0.07		
	SD, SE	0.059, 0.026		
	MEDIAN	0.06		
	MIN, MAX	0.04, 0.18		
	5%, 95%	0.04, 0.18		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 13 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	7	8	0.0015
	MEAN, GEO MEAN	33.31, 31.47	10.42, 9.82	
	SD, SE	13.624, 5.150	4.045, 1.430	
	MEDIAN	29.87	9.68	
	MIN, MAX	19.77, 62.63	6.74, 18.39	
	5%, 95%	19.77, 62.63	6.74, 18.39	
	# of BLQ/ALQ Values	0/0	0/0	
Week 6	N	7	8	0.0032
	MEAN, GEO MEAN	32.57, 28.28	11.30, 10.58	
	SD, SE	21.523, 8.135	4.479, 1.584	
	MEDIAN	27.83	9.93	
	MIN, MAX	16.85, 78.25	6.90, 19.24	
	5%, 95%	16.85, 78.25	6.90, 19.24	
	# of BLQ/ALQ Values	0/0	0/0	
Overall [*]	N	8	8	0.0009
	MEAN, GEO MEAN	32.48, 30.80	10.86, 10.35	
	SD, SE	11.676, 4.128	3.648, 1.290	
	MEDIAN	29.20	9.86	
	MIN, MAX	18.31, 54.06	6.99, 16.69	
	5%, 95%	18.31, 54.06	6.99, 16.69	

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-1
Statistical Comparison Between Smokers and Non-Smokers of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 14 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	7	
	MEAN, GEO MEAN	4.61, 3.07	
	SD, SE	5.135, 1.941	
	MEDIAN	2.30	
	MIN, MAX	1.00, 15.66	
	5%, 95%	1.00, 15.66	
	# of BLQ/ALQ Values	0/0	
Week 6	N	7	
	MEAN, GEO MEAN	7.72, 2.20	
	SD, SE	2.048, 0.774	
	MEDIAN	2.43	
	MIN, MAX	0.89, 6.96	
	5%, 95%	0.89, 6.96	
	# of BLQ/ALQ Values	0/0	
Overall*	N	8	
	MEAN, GEO MEAN	3.62, 2.81	
	SD, SE	3.281, 1.160	
	MEDIAN	2.59	
	MIN, MAX	1.33, 11.31	
	5%, 95%	1.33, 11.31	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 264)

Biomarker: NNAL (pg/24hr)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	249287.700, 181853.367	11565.751, 10175.939	
	SD, SE	180186.7708, 25482.2575	6083.1888, 754.5267	
	MEDIAN	224364.000	9420.000	
	MIN, MAX	8460.000, 852355.000	3180.000, 30796.800	
	5%, 95%	23940.000, 649460.000	4800.000, 22800.000	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	278384.265, 210748.456	14031.600, 12142.720	
	SD, SE	174391.9368, 25712.6883	9362.8824, 1161.3226	
	MEDIAN	241481.000	12000.000	
	MIN, MAX	6288.000, 781704.000	4500.000, 57240.000	
	5%, 95%	52440.000, 558700.000	5940.000, 28440.000	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	259455.192, 199546.451	12798.675, 11568.878	
	SD, SE	160409.3654, 22685.3100	6104.9573, 757.2268	
	MEDIAN	239327.000	11190.000	
	MIN, MAX	7374.000, 589956.000	3840.000, 32310.000	
	5%, 95%	47776.000, 584078.900	6450.000, 24998.400	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL (pmol/24hr)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1191.595, 869.259	55.284, 48.641	
	SD, SE	861.2928, 121.8052	29.0777, 3.6066	
	MEDIAN	1072.460	45.028	
	MIN, MAX	40.439, 4074.257	15.200, 147.209	
	5%, 95%	114.433, 3104.419	22.944, 108.984	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1330.677, 1007.378	67.071, 58.042	
	SD, SE	833.5934, 122.9066	44.7546, 5.5511	
	MEDIAN	1154.279	57.360	
	MIN, MAX	30.057, 3736.545	21.510, 273.607	
	5%, 95%	250.663, 2670.586	28.393, 135.943	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1240.196, 953.832	61.178, 55.299	
	SD, SE	766.7568, 108.4358	29.1817, 3.6195	
	MEDIAN	1143.984	53.488	
	MIN, MAX	35.248, 2819.990	18.355, 154.442	
	5%, 95%	228.369, 2791.897	30.831, 119.493	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL (ng/24hr/cigarette per day)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50		NA
	MEAN, GEO MEAN	18139.155, 13969.400		
	SD, SE	15044.5776, 2127.6246		
	MEDIAN	13949.909		
	MIN, MAX	2820.000, 85235.500		
	5%, 95%	5471.667, 46530.000		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	20247.891, 16799.465		
	SD, SE	12691.7845, 1871.3015		
	MEDIAN	16864.236		
	MIN, MAX	2096.000, 64500.000		
	5%, 95%	6486.000, 41592.667		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	19273.807, 15968.329		
	SD, SE	12317.2616, 1741.9238		
	MEDIAN	14798.998		
	MIN, MAX	2458.000, 62355.425		
	5%, 95%	5079.000, 42648.800		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 264)

Biomarker: NNAL (pmol/24hr/cigarette per day) Analytical Lab: Madison				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50		NA
	MEAN, GEO MEAN	86.705, 66.774		
	SD, SE	71.9131, 10.1701		
	MEDIAN	66.681		
	MIN, MAX	13.480, 407.426		
	5%, 95%	26.155, 222.413		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	96.785, 80.301		
	SD, SE	60.6667, 8.9448		
	MEDIAN	80.612		
	MIN, MAX	10.019, 308.310		
	5%, 95%	31.003, 198.813		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	92.129, 76.329		
	SD, SE	58.8765, 8.3264		
	MEDIAN	70.740		
	MIN, MAX	11.750, 298.059		
	5%, 95%	24.278, 203.862		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL (pg/mg Creatinine)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	219.163, 150.676	8.498, 7.145	
	SD, SE	181.7279, 25.7002	5.1547, 0.6394	
	MEDIAN	178.751	7.823	
	MIN, MAX	7.958, 813.359	1.932, 29.814	
	5%, 95%	13.730, 612.755	2.911, 17.143	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	226.894, 168.981	10.253, 8.514	
	SD, SE	159.6468, 23.5386	6.4647, 0.8019	
	MEDIAN	194.555	9.259	
	MIN, MAX	5.525, 724.324	2.158, 30.264	
	5%, 95%	47.240, 547.012	2.923, 23.715	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	223.061, 162.757	9.376, 8.147	
	SD, SE	167.5167, 23.6904	4.8825, 0.6056	
	MEDIAN	185.127	8.674	
	MIN, MAX	6.742, 768.842	2.364, 23.043	
	5%, 95%	34.373, 535.268	3.185, 18.495	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL (pmol/mg Creatinine)		Analytical Lab: Madison		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1.048, 0.720	0.041, 0.034	
	SD, SE	0.8687, 0.1229	0.0247, 0.0031	
	MEDIAN	0.855	0.037	
	MIN, MAX	0.038, 3.888	0.009, 0.143	
	5%, 95%	0.066, 2.929	0.014, 0.082	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1.085, 0.807	0.049, 0.041	
	SD, SE	0.7631, 0.1125	0.0308, 0.0038	
	MEDIAN	0.930	0.044	
	MIN, MAX	0.026, 3.462	0.010, 0.145	
	5%, 95%	0.226, 2.615	0.014, 0.113	
	# of BLQ/ALQ Values	1/0	61/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	1.066, 0.778	0.045, 0.039	
	SD, SE	0.8008, 0.1132	0.0233, 0.0029	
	MEDIAN	0.885	0.042	
	MIN, MAX	0.032, 3.675	0.011, 0.110	
	5%, 95%	0.164, 2.559	0.015, 0.088	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL ((pg/mg Creatinine)/cigarette per day)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50		NA
	MEAN, GEO MEAN	17.186, 11.574		
	SD, SE	22.5070, 3.1830		
	MEDIAN	11.512		
	MIN, MAX	2.653, 153.410		
	5%, 95%	3.199, 40.850		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	17.401, 13.470		
	SD, SE	14.5069, 2.1389		
	MEDIAN	12.185		
	MIN, MAX	1.842, 69.200		
	5%, 95%	4.470, 55.549		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	17.523, 13.046		
	SD, SE	16.9853, 2.4021		
	MEDIAN	11.915		
	MIN, MAX	2.248, 104.480		
	5%, 95%	4.078, 40.850		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 264)

Biomarker: NNAL ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50		NA
	MEAN, GEO MEAN	0.082, 0.055		
	SD, SE	0.1075, 0.0152		
	MEDIAN	0.055		
	MIN, MAX	0.013, 0.733		
	5%, 95%	0.015, 0.195		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.083, 0.064		
	SD, SE	0.0694, 0.0102		
	MEDIAN	0.058		
	MIN, MAX	0.009, 0.331		
	5%, 95%	0.021, 0.266		
	# of BLQ/ALQ Values	1/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	0.084, 0.063		
	SD, SE	0.0812, 0.0115		
	MEDIAN	0.057		
	MIN, MAX	0.011, 0.500		
	5%, 95%	0.020, 0.195		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 9 of 264)

Biomarker: NNAL (pg/mL)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	150.0, 106.4	6.4, 6.2	
	SD, SE	107.23, 15.16	1.89, 0.23	
	MEDIAN	136.4	6.0	
	MIN, MAX	6.0, 484.5	6.0, 20.3	
	5%, 95%	11.4, 347.9	6.0, 8.5	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	161.2, 123.5	7.3, 6.5	
	SD, SE	109.14, 16.09	6.31, 0.78	
	MEDIAN	144.2	6.0	
	MIN, MAX	6.0, 485.1	6.0, 42.4	
	5%, 95%	28.2, 405.1	6.0, 10.5	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	153.7, 118.3	6.9, 6.5	
	SD, SE	101.02, 14.29	3.26, 0.40	
	MEDIAN	138.9	6.0	
	MIN, MAX	6.0, 474.5	6.0, 24.2	
	5%, 95%	20.9, 351.6	6.0, 11.4	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 10 of 264)

Biomarker: NNAL (pmol/L)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	717.2, 508.7	30.5, 29.8	
	SD, SE	512.56, 72.49	9.01, 1.12	
	MEDIAN	652.0	28.7	
	MIN, MAX	28.7, 2315.9	28.7, 97.0	
	5%, 95%	54.5, 1663.0	28.7, 40.6	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	770.5, 590.3	35.0, 31.2	
	SD, SE	521.68, 76.92	30.16, 3.74	
	MEDIAN	689.0	28.7	
	MIN, MAX	28.7, 2318.8	28.7, 202.7	
	5%, 95%	134.8, 1936.4	28.7, 50.2	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	734.7, 565.3	32.8, 31.1	
	SD, SE	482.89, 68.29	15.56, 1.93	
	MEDIAN	663.9	28.7	
	MIN, MAX	28.7, 2268.1	28.7, 115.7	
	5%, 95%	99.9, 1680.7	28.7, 54.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 11 of 264)

Biomarker: NNAL ((pg/mL)/cigarette per day)		Analytical Lab: Madison	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	11.0, 8.2	
	SD, SE	9.18, 1.30	
	MEDIAN	7.9	
	MIN, MAX	1.4, 47.0	
	5%, 95%	2.0, 27.8	
	# of BLQ/ALQ Values	2/0	
Week 3	N	46	
	MEAN, GEO MEAN	12.9, 9.8	
	SD, SE	10.89, 1.61	
	MEDIAN	10.3	
	MIN, MAX	2.0, 58.2	
	5%, 95%	2.8, 31.2	
	# of BLQ/ALQ Values	1/0	
Overall*	N	50	
	MEAN, GEO MEAN	12.2, 9.5	
	SD, SE	9.72, 1.37	
	MEDIAN	8.9	
	MIN, MAX	2.0, 47.0	
	5%, 95%	2.7, 36.7	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 12 of 264)

Biomarker: NNAL ((pmol/L)/cigarette per day)		Analytical Lab: Madison	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	52.5, 39.1	
	SD, SE	43.87, 6.20	
	MEDIAN	37.9	
	MIN, MAX	6.5, 224.7	
	5%, 95%	9.6, 132.6	
	# of BLQ/ALQ Values	2/0	
Week 3	N	46	
	MEAN, GEO MEAN	61.7, 47.1	
	SD, SE	52.02, 7.67	
	MEDIAN	49.0	
	MIN, MAX	9.6, 278.0	
	5%, 95%	13.5, 148.9	
	# of BLQ/ALQ Values	1/0	
Overall*	N	50	
	MEAN, GEO MEAN	58.1, 45.1	
	SD, SE	46.43, 6.57	
	MEDIAN	42.3	
	MIN, MAX	9.6, 224.7	
	5%, 95%	12.7, 175.1	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 13 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/24hr)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	860758.551, 585425.280	14520.477, 10879.233	
	SD, SE	613472.2046, 87638.8864	22133.4597, 2745.3178	
	MEDIAN	785030.000	10140.000	
	MIN, MAX	8460.000, 2307613.000	3180.000, 181986.000	
	5%, 95%	37125.000, 2084332.500	4680.000, 21000.000	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	914457.937, 627898.806	14369.154, 12281.453	
	SD, SE	709365.3233, 104590.2109	10422.0126, 1292.6916	
	MEDIAN	783064.000	12000.000	
	MIN, MAX	6288.000, 4046406.000	4500.000, 61490.000	
	5%, 95%	97520.000, 1964160.000	6408.000, 28440.000	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	874401.621, 615371.996	14444.815, 11969.312	
	SD, SE	592615.0179, 83808.4196	12990.5012, 1611.2734	
	MEDIAN	839769.000	11070.000	
	MIN, MAX	7374.000, 2468208.000	3840.000, 97218.000	
	5%, 95%	66085.000, 2080140.250	6400.000, 30583.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 14 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/24hr) Analytical Lab: Madison				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	4114.426, 2798.333	69.408, 52.003	
	SD, SE	2932.3970, 418.9139	105.7979, 13.1226	
	MEDIAN	3752.443	48.469	
	MIN, MAX	40.439, 11030.390	15.200, 869.893	
	5%, 95%	177.458, 9963.109	22.370, 100.380	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	4371.109, 3001.357	68.685, 58.705	
	SD, SE	3390.7663, 499.9412	49.8172, 6.1791	
	MEDIAN	3743.046	57.360	
	MIN, MAX	30.057, 19341.821	21.510, 293.922	
	5%, 95%	466.146, 9388.685	30.630, 135.943	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^a	N	50	65	<.0001
	MEAN, GEO MEAN	4179.640, 2941.479	69.046, 57.214	
	SD, SE	2832.6997, 400.6042	62.0946, 7.7019	
	MEDIAN	4014.096	52.915	
	MIN, MAX	35.248, 11798.035	18.355, 464.702	
	5%, 95%	315.887, 9943.070	30.592, 146.187	

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pg/24hr)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	56456.734, 44404.705		
	SD, SE	38952.1879, 5564.5983		
	MEDIAN	50477.857		
	MIN, MAX	2820.000, 176718.500		
	5%, 95%	12565.000, 153840.867		
	# of BLQ/ALQ Values	1/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	62625.596, 50051.917		
	SD, SE	40626.0676, 5989.9869		
	MEDIAN	51940.813		
	MIN, MAX	2096.000, 192686.000		
	5%, 95%	18154.500, 138353.600		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	59627.475, 49291.845		
	SD, SE	34052.5998, 4815.7648		
	MEDIAN	51637.690		
	MIN, MAX	2458.000, 154712.800		
	5%, 95%	16521.250, 132624.738		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pmol/24hr)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	269.863, 212.255		
	SD, SE	186.1914, 26.5988		
	MEDIAN	241.284		
	MIN, MAX	13.480, 844.714		
	5%, 95%	60.061, 735.359		
	# of BLQ/ALQ Values	1/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	299.350, 239.248		
	SD, SE	194.1926, 28.6321		
	MEDIAN	248.277		
	MIN, MAX	10.019, 921.039		
	5%, 95%	86.779, 661.330		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	285.020, 235.616		
	SD, SE	162.7713, 23.0193		
	MEDIAN	246.829		
	MIN, MAX	11.750, 739.527		
	5%, 95%	78.972, 633.946		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pg/mg Creatinine)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	738.054, 487.673	10.558, 7.638	
	SD, SE	585.2483, 83.6069	16.3892, 2.0328	
	MEDIAN	625.442	8.915	
	MIN, MAX	7.958, 2575.145	1.932, 134.956	
	5%, 95%	30.892, 2010.238	2.683, 17.699	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	721.933, 503.456	10.876, 8.612	
	SD, SE	524.1048, 77.2750	9.0374, 1.1210	
	MEDIAN	580.019	8.380	
	MIN, MAX	5.525, 2275.640	2.158, 53.767	
	5%, 95%	65.031, 2004.781	2.923, 30.000	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	726.768, 500.586	10.717, 8.491	
	SD, SE	532.2826, 75.2761	9.7162, 1.2051	
	MEDIAN	617.105	8.438	
	MIN, MAX	6.742, 2250.747	2.131, 70.371	
	5%, 95%	43.687, 1877.496	3.508, 27.562	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pmol/mg Creatinine)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	3.528, 2.331	0.050, 0.036	
	SD, SE	2.7975, 0.3996	0.0783, 0.0097	
	MEDIAN	2.990	0.043	
	MIN, MAX	0.038, 12.309	0.009, 0.645	
	5%, 95%	0.148, 9.609	0.013, 0.085	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	3.451, 2.406	0.052, 0.041	
	SD, SE	2.5053, 0.3694	0.0432, 0.0054	
	MEDIAN	2.773	0.040	
	MIN, MAX	0.026, 10.878	0.010, 0.257	
	5%, 95%	0.311, 9.583	0.014, 0.143	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3.474, 2.393	0.051, 0.041	
	SD, SE	2.5443, 0.3598	0.0465, 0.0058	
	MEDIAN	2.950	0.041	
	MIN, MAX	0.032, 10.759	0.010, 0.337	
	5%, 95%	0.209, 8.975	0.017, 0.132	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pg/mg Creatinine)/cigarette per day) Analytical Lab: Madison			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	49	
	MEAN, GEO MEAN	53.989, 36.990	
	SD, SE	73.1881, 10.4554	
	MEDIAN	40.489	
	MIN, MAX	2.653, 515.029	
	5%, 95%	8.053, 116.939	
	# of BLQ/ALQ Values	1/0	
Week 3	N	46	
	MEAN, GEO MEAN	52.624, 40.132	
	SD, SE	44.1283, 6.5064	
	MEDIAN	39.373	
	MIN, MAX	1.842, 235.969	
	5%, 95%	16.258, 155.193	
	# of BLQ/ALQ Values	1/0	
Overall*	N	50	
	MEAN, GEO MEAN	53.613, 40.164	
	SD, SE	54.9019, 7.7643	
	MEDIAN	41.836	
	MIN, MAX	2.248, 375.499	
	5%, 95%	13.016, 131.185	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	0.258, 0.177		
	SD, SE	0.3498, 0.0500		
	MEDIAN	0.194		
	MIN, MAX	0.013, 2.462		
	5%, 95%	0.039, 0.559		
	# of BLQ/ALQ Values	1/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.252, 0.192		
	SD, SE	0.2109, 0.0311		
	MEDIAN	0.189		
	MIN, MAX	0.009, 1.128		
	5%, 95%	0.078, 0.742		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	0.257, 0.193		
	SD, SE	0.2624, 0.0371		
	MEDIAN	0.200		
	MIN, MAX	0.011, 1.795		
	5%, 95%	0.063, 0.627		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pg/mL)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	546.8, 341.2	9.5, 6.7	
	SD, SE	468.94, 66.99	22.78, 2.83	
	MEDIAN	475.2	6.0	
	MIN, MAX	6.0, 2045.7	6.0, 185.7	
	5%, 95%	16.5, 1604.2	6.0, 8.8	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	552.8, 367.9	7.4, 6.6	
	SD, SE	487.35, 71.86	6.14, 0.76	
	MEDIAN	426.6	6.0	
	MIN, MAX	6.0, 2223.3	6.0, 47.3	
	5%, 95%	53.0, 1721.9	6.0, 11.9	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	542.5, 366.0	8.5, 6.8	
	SD, SE	427.04, 60.39	12.25, 1.52	
	MEDIAN	433.9	6.0	
	MIN, MAX	6.0, 1663.1	6.0, 95.9	
	5%, 95%	34.8, 1471.5	6.0, 11.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pmol/L)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	65	<.0001
	MEAN, GEO MEAN	2613.5, 1631.1	45.7, 31.9	
	SD, SE	2241.53, 320.22	108.87, 13.50	
	MEDIAN	2271.5	28.7	
	MIN, MAX	28.7, 9778.4	28.7, 887.6	
	5%, 95%	78.9, 7668.1	28.7, 42.1	
	# of BLQ/ALQ Values	1/0	58/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	2642.5, 1758.6	35.3, 31.6	
	SD, SE	2329.54, 343.47	29.34, 3.64	
	MEDIAN	2038.9	28.7	
	MIN, MAX	28.7, 10627.4	28.7, 226.1	
	5%, 95%	253.3, 8230.7	28.7, 56.9	
	# of BLQ/ALQ Values	1/0	58/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	2592.9, 1749.4	40.5, 32.5	
	SD, SE	2041.22, 288.67	58.54, 7.26	
	MEDIAN	2074.0	28.7	
	MIN, MAX	28.7, 7949.4	28.7, 458.2	
	5%, 95%	166.1, 7033.6	28.7, 56.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pg/mL)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	36.0, 25.9		
	SD, SE	29.20, 4.17		
	MEDIAN	27.0		
	MIN, MAX	2.0, 128.6		
	5%, 95%	6.0, 95.6		
	# of BLQ/ALQ Values	1/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	41.9, 29.3		
	SD, SE	41.76, 6.16		
	MEDIAN	24.0		
	MIN, MAX	2.0, 247.1		
	5%, 95%	10.0, 100.6		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	39.2, 29.2		
	SD, SE	31.74, 4.49		
	MEDIAN	27.8		
	MIN, MAX	2.0, 168.1		
	5%, 95%	8.7, 98.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pmol/L)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	172.1, 123.7		
	SD, SE	139.58, 19.94		
	MEDIAN	129.3		
	MIN, MAX	9.6, 614.6		
	5%, 95%	28.6, 456.7		
	# of BLQ/ALQ Values	1/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	200.3, 140.2		
	SD, SE	199.60, 29.43		
	MEDIAN	114.5		
	MIN, MAX	9.6, 1180.9		
	5%, 95%	47.7, 481.1		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	187.4, 139.7		
	SD, SE	151.69, 21.45		
	MEDIAN	132.8		
	MIN, MAX	9.6, 803.4		
	5%, 95%	41.5, 468.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide (pmol/L)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	61	<.0001
	MEAN, GEO MEAN	1889.1, NA	18.1, NA	
	SD, SE	1803.06, 257.58	112.36, 14.39	
	MEDIAN	1564.5	0.0	
	MIN, MAX	0.0, 7462.5	0.0, 859.0	
	5%, 95%	35.9, 5782.8	0.0, 13.4	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	63	<.0001
	MEAN, GEO MEAN	1872.0, NA	3.8, NA	
	SD, SE	1907.93, 281.31	15.16, 1.91	
	MEDIAN	1352.5	0.0	
	MIN, MAX	0.0, 9536.6	0.0, 99.9	
	5%, 95%	35.4, 5911.9	0.0, 28.2	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1859.5, NA	10.3, NA	
	SD, SE	1623.98, 229.67	55.10, 6.83	
	MEDIAN	1521.7	0.0	
	MIN, MAX	0.0, 5778.3	0.0, 429.5	
	5%, 95%	29.9, 5668.4	0.0, 28.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide ((pmol/L)/cigarette per day) Analytical Lab: Madison				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49		NA
	MEAN, GEO MEAN	119.6, NA		
	SD, SE	103.95, 14.85		
	MEDIAN	85.8		
	MIN, MAX	0.0, 481.9		
	5%, 95%	16.1, 339.2		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	138.6, NA		
	SD, SE	154.18, 22.73		
	MEDIAN	79.1		
	MIN, MAX	0.0, 902.9		
	5%, 95%	8.9, 350.2		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	129.5, NA		
	SD, SE	112.33, 15.89		
	MEDIAN	90.0		
	MIN, MAX	0.0, 601.0		
	5%, 95%	10.4, 345.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide (pmol/24hr)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	49	61	<.0001
	MEAN, GEO MEAN	2908.931, NA	18.258, NA	
	SD, SE	2273.5232, 324.7890	109.6835, 14.0435	
	MEDIAN	2416.280	0.000	
	MIN, MAX	0.000, 8788.668	0.000, 841.820	
	5%, 95%	98.725, 7630.840	0.000, 21.417	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	63	<.0001
	MEAN, GEO MEAN	3040.444, NA	7.137, NA	
	SD, SE	2849.3120, 420.1081	29.7623, 3.7497	
	MEDIAN	2468.524	0.000	
	MIN, MAX	0.000, 17356.612	0.000, 168.831	
	5%, 95%	65.136, 6821.100	0.000, 36.120	
	# of BLQ/ALQ Values	1/0	61/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	2940.092, NA	12.026, NA	
	SD, SE	2262.4910, 319.9646	55.0893, 6.8330	
	MEDIAN	2635.937	0.000	
	MIN, MAX	0.000, 10073.384	0.000, 420.910	
	5%, 95%	59.593, 7804.884	0.000, 80.217	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide ((pmol/24hr)/cigarette per day)		Analytical Lab: Madison	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	49	
	MEAN, GEO MEAN	182.878, NA	
	SD, SE	131.3278, 18.7611	
	MEDIAN	156.941	
	MIN, MAX	0.000, 585.911	
	5%, 95%	33.903, 437.301	
	# of BLQ/ALQ Values	2/0	
Week 3	N	46	
	MEAN, GEO MEAN	202.567, NA	
	SD, SE	154.2054, 22.7363	
	MEDIAN	161.451	
	MIN, MAX	0.000, 826.505	
	5%, 95%	16.284, 505.646	
	# of BLQ/ALQ Values	1/0	
Overall*	N	50	
	MEAN, GEO MEAN	192.984, NA	
	SD, SE	121.2762, 17.1510	
	MEDIAN	166.137	
	MIN, MAX	0.000, 539.902	
	5%, 95%	27.239, 476.665	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide (pmol/mg Creatinine)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	61	<.0001
	MEAN, GEO MEAN	2.466, NA	0.013, NA	
	SD, SE	2.0265, 0.2895	0.0808, 0.0103	
	MEDIAN	2.190	0.000	
	MIN, MAX	0.000, 8.643	0.000, 0.624	
	5%, 95%	0.082, 7.656	0.000, 0.009	
	# of BLQ/ALQ Values	2/0	61/0	
Week 3	N	46	63	<.0001
	MEAN, GEO MEAN	2.366, NA	0.006, NA	
	SD, SE	1.9608, 0.2891	0.0271, 0.0034	
	MEDIAN	1.823	0.000	
	MIN, MAX	0.000, 9.761	0.000, 0.171	
	5%, 95%	0.043, 6.216	0.000, 0.019	
	# of BLQ/ALQ Values	1/0	61/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	2.409, NA	0.009, NA	
	SD, SE	1.8649, 0.2637	0.0412, 0.0051	
	MEDIAN	1.986	0.000	
	MIN, MAX	0.000, 7.312	0.000, 0.312	
	5%, 95%	0.051, 6.478	0.000, 0.065	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide ((pmol/mg Creatinine)/cigarette per day) Analytical Lab: Madison				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49		NA
	MEAN, GEO MEAN	0.175, NA		
	SD, SE	0.2469, 0.0353		
	MEDIAN	0.119		
	MIN, MAX	0.000, 1.729		
	5%, 95%	0.022, 0.364		
	# of BLQ/ALQ Values	2/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.168, NA		
	SD, SE	0.1548, 0.0228		
	MEDIAN	0.119		
	MIN, MAX	0.000, 0.862		
	5%, 95%	0.011, 0.465		
	# of BLQ/ALQ Values	1/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	0.173, NA		
	SD, SE	0.1885, 0.0267		
	MEDIAN	0.133		
	MIN, MAX	0.000, 1.296		
	5%, 95%	0.023, 0.364		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (µg/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1779.837, 1321.434	3.165, 2.104	
	SD, SE	1152.0055, 162.9182	4.4410, 0.5508	
	MEDIAN	1795.815	1.930	
	MIN, MAX	26.790, 6435.660	0.530, 27.900	
	5%, 95%	308.979, 3580.185	0.780, 12.160	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1817.746, 1365.985	3.684, 2.287	
	SD, SE	1072.6598, 153.2371	7.4411, 0.9230	
	MEDIAN	1731.974	2.160	
	MIN, MAX	13.950, 4366.890	0.625, 59.280	
	5%, 95%	226.118, 3766.020	0.815, 9.804	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1953.822, 1428.929	2.968, 2.232	
	SD, SE	1298.5750, 191.4644	3.6920, 0.4579	
	MEDIAN	1633.047	2.050	
	MIN, MAX	6.393, 5162.740	0.750, 25.870	
	5%, 95%	354.936, 4856.040	1.068, 7.188	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1822.896, 1402.089	3.272, 2.312	
	SD, SE	1058.1876, 149.6503	4.4212, 0.5484	
	MEDIAN	1695.438	2.143	
	MIN, MAX	15.711, 4483.278	0.787, 30.043	
	5%, 95%	374.266, 3774.690	1.092, 12.202	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 32 of 264)

Biomarker: Cotinine (nmol/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	10100.578, 7499.138	17.961, 11.943	
	SD, SE	6537.6311, 924.5607	25.2025, 3.1260	
	MEDIAN	10191.251	10.953	
	MIN, MAX	152.033, 36522.371	3.008, 158.333	
	5%, 95%	1753.456, 20317.550	4.427, 69.008	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	10315.706, 7751.966	20.906, 12.977	
	SD, SE	6087.3442, 869.6206	42.2284, 5.2378	
	MEDIAN	9828.952	12.258	
	MIN, MAX	79.166, 24782.101	3.547, 336.414	
	5%, 95%	1283.220, 21372.164	4.625, 55.638	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	11087.937, 8109.168	16.845, 12.667	
	SD, SE	7369.4133, 1086.5607	20.9521, 2.5988	
	MEDIAN	9267.542	11.634	
	MIN, MAX	36.280, 29298.550	4.256, 146.812	
	5%, 95%	2014.262, 27558.027	6.061, 40.792	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	10344.938, 7956.855	18.571, 13.119	
	SD, SE	6005.2150, 849.2657	25.0903, 3.1121	
	MEDIAN	9621.607	12.163	
	MIN, MAX	89.160, 25442.605	4.464, 170.496	
	5%, 95%	2123.957, 21421.368	6.195, 69.245	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 33 of 264)

Biomarker: Cotinine ((μ g/24hr)/cigarette per day) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50		NA
	MEAN, GEO MEAN	130.879, 101.508		
	SD, SE	108.2704, 15.3117		
	MEDIAN	98.981		
	MIN, MAX	8.930, 643.566		
	5%, 95%	29.911, 304.113		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	155.721, 110.210		
	SD, SE	190.7348, 27.2478		
	MEDIAN	114.398		
	MIN, MAX	4.650, 1308.045		
	5%, 95%	32.303, 342.365		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	142.739, 113.905		
	SD, SE	86.5808, 12.7656		
	MEDIAN	118.942		
	MIN, MAX	2.131, 335.938		
	5%, 95%	46.306, 325.744		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	141.944, 113.039		
	SD, SE	111.7605, 15.8053		
	MEDIAN	103.857		
	MIN, MAX	5.237, 671.319		
	5%, 95%	47.120, 299.233		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 34 of 264)

Biomarker: Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	742.740, 576.060		
	SD, SE	614.4343, 86.8941		
	MEDIAN	561.716		
	MIN, MAX	50.678, 3652.237		
	5%, 95%	169.746, 1725.843		
Week 2	# of BLQ/ALQ Values	0/0		NA
	N	49		
	MEAN, GEO MEAN	883.715, 625.443		
	SD, SE	1082.4199, 154.6314		
	MEDIAN	649.206		
	MIN, MAX	26.389, 7423.156		
Week 3	5%, 95%	183.317, 1942.924		NA
	# of BLQ/ALQ Values	0/0		
	N	46		
	MEAN, GEO MEAN	810.046, 646.409		
	SD, SE	491.3460, 72.4450		
	MEDIAN	674.991		
Overall*	MIN, MAX	12.093, 1906.445		NA
	5%, 95%	262.788, 1848.600		
	# of BLQ/ALQ Values	0/0		
	N	50		
	MEAN, GEO MEAN	805.529, 641.498		
	SD, SE	634.2410, 89.6952		
Overall*	MEDIAN	589.388		NA
	MIN, MAX	29.720, 3809.735		
	5%, 95%	267.406, 1698.146		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (µg/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1.607, 1.095	0.002, NA	
	SD, SE	1.2214, 0.1727	0.0030, 0.0004	
	MEDIAN	1.401	0.001	
	MIN, MAX	0.025, 5.808	0.000, 0.020	
	5%, 95%	0.203, 3.903	0.000, 0.009	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1.474, 1.055	0.003, NA	
	SD, SE	1.0867, 0.1552	0.0070, 0.0009	
	MEDIAN	1.263	0.002	
	MIN, MAX	0.016, 5.177	0.000, 0.057	
	5%, 95%	0.148, 3.337	0.000, 0.007	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1.609, 1.147	0.002, NA	
	SD, SE	1.1859, 0.1749	0.0022, 0.0003	
	MEDIAN	1.333	0.002	
	MIN, MAX	0.006, 5.186	0.000, 0.014	
	5%, 95%	0.383, 4.005	0.001, 0.005	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1.575, 1.138	0.002, NA	
	SD, SE	1.1231, 0.1588	0.0035, 0.0004	
	MEDIAN	1.305	0.002	
	MIN, MAX	0.016, 4.572	0.000, 0.026	
	5%, 95%	0.266, 3.886	0.001, 0.007	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 36 of 264)

Biomarker: Cotinine (nmol/mg Creatinine)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	9.121, 6.214	0.013, NA	
	SD, SE	6.9314, 0.9802	0.0173, 0.0021	
	MEDIAN	7.951	0.006	
	MIN, MAX	0.142, 32.960	0.000, 0.114	
	5%, 95%	1.152, 22.150	0.000, 0.051	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	8.365, 5.987	0.017, NA	
	SD, SE	6.1668, 0.8810	0.0397, 0.0049	
	MEDIAN	7.168	0.011	
	MIN, MAX	0.091, 29.379	0.000, 0.323	
	5%, 95%	0.840, 18.937	0.000, 0.040	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	9.133, 6.511	0.012, NA	
	SD, SE	6.7302, 0.9923	0.0124, 0.0015	
	MEDIAN	7.565	0.011	
	MIN, MAX	0.034, 29.431	0.000, 0.079	
	5%, 95%	2.174, 22.728	0.006, 0.028	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	8.937, 6.454	0.014, NA	
	SD, SE	6.3738, 0.9014	0.0196, 0.0024	
	MEDIAN	7.403	0.009	
	MIN, MAX	0.089, 25.944	0.000, 0.149	
	5%, 95%	1.510, 22.053	0.004, 0.038	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 37 of 264)

Biomarker: Cotinine ((µg/rmg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	0.129, 0.084	
	SD, SE	0.1723, 0.0244	
	MEDIAN	0.082	
	MIN, MAX	0.008, 1.162	
	5%, 95%	0.021, 0.366	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	0.154, 0.085	
	SD, SE	0.3622, 0.0517	
	MEDIAN	0.076	
	MIN, MAX	0.005, 2.589	
	5%, 95%	0.023, 0.303	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	0.125, 0.091	
	SD, SE	0.1146, 0.0169	
	MEDIAN	0.100	
	MIN, MAX	0.002, 0.580	
	5%, 95%	0.032, 0.321	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	0.137, 0.092	
	SD, SE	0.2027, 0.0287	
	MEDIAN	0.094	
	MIN, MAX	0.005, 1.432	
	5%, 95%	0.034, 0.311	
			NA

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 38 of 264)

Biomarker: Cotinine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	0.732, 0.477	
	SD, SE	0.9777, 0.1383	
	MEDIAN	0.462	
	MIN, MAX	0.047, 6.592	
	5%, 95%	0.119, 2.078	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	0.871, 0.483	
	SD, SE	2.0554, 0.2936	
	MEDIAN	0.429	
	MIN, MAX	0.030, 14.690	
	5%, 95%	0.129, 1.721	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	0.709, 0.519	
	SD, SE	0.6501, 0.0959	
	MEDIAN	0.565	
	MIN, MAX	0.011, 3.292	
	5%, 95%	0.182, 1.821	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	0.776, 0.521	
	SD, SE	1.1504, 0.1627	
	MEDIAN	0.533	
	MIN, MAX	0.029, 8.127	
	5%, 95%	0.190, 1.767	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 39 of 264)

Biomarker: Cotinine (ng/mL)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1029.4, 773.3	1.7, 1.3	
	SD, SE	619.01, 87.54	2.09, 0.26	
	MEDIAN	919.4	1.0	
	MIN, MAX	18.2, 2626.8	1.0, 14.1	
	5%, 95%	226.0, 2263.4	1.0, 4.8	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1154.8, 883.0	1.9, 1.3	
	SD, SE	788.02, 112.57	2.91, 0.36	
	MEDIAN	975.4	1.0	
	MIN, MAX	15.5, 4778.6	1.0, 20.8	
	5%, 95%	221.4, 2343.3	1.0, 4.1	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1082.9, 837.2	1.5, 1.2	
	SD, SE	632.01, 93.19	2.42, 0.30	
	MEDIAN	998.4	1.0	
	MIN, MAX	6.1, 2858.1	1.0, 19.9	
	5%, 95%	257.2, 2346.7	1.0, 2.8	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1076.8, 846.7	1.7, 1.3	
	SD, SE	616.60, 87.20	2.10, 0.26	
	MEDIAN	970.2	1.0	
	MIN, MAX	13.5, 3090.2	1.0, 13.9	
	5%, 95%	275.9, 1962.5	1.0, 4.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 40 of 264)

Biomarker: Cotinine (nmol/L)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	5842.0, 4388.4	9.6, 7.3	
	SD, SE	3512.90, 496.80	11.88, 1.47	
	MEDIAN	5217.3	5.7	
	MIN, MAX	103.3, 14907.1	5.7, 80.0	
	5%, 95%	1282.6, 12844.8	5.7, 27.2	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	6553.5, 5010.8	10.6, 7.6	
	SD, SE	4472.01, 638.86	16.49, 2.04	
	MEDIAN	5535.4	5.7	
	MIN, MAX	88.0, 27118.6	5.7, 118.0	
	5%, 95%	1256.4, 13298.2	5.7, 23.3	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	6145.2, 4751.3	8.7, 6.8	
	SD, SE	3586.67, 528.83	13.73, 1.70	
	MEDIAN	5665.7	5.7	
	MIN, MAX	34.6, 16219.7	5.7, 112.9	
	5%, 95%	1459.6, 13317.5	5.7, 15.9	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	6110.8, 4805.3	9.6, 7.5	
	SD, SE	3499.18, 494.86	11.94, 1.48	
	MEDIAN	5505.8	5.7	
	MIN, MAX	76.8, 17537.1	5.7, 78.7	
	5%, 95%	1566.0, 11137.0	5.7, 23.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	74.4, 59.4		
	SD, SE	52.18, 7.38		
	MEDIAN	58.2		
	MIN, MAX	6.3, 262.7		
	5%, 95%	15.1, 188.6		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	98.3, 71.2		
	SD, SE	121.43, 17.35		
	MEDIAN	67.8		
	MIN, MAX	5.2, 843.9		
	5%, 95%	29.6, 238.9		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	90.8, 66.7		
	SD, SE	91.22, 13.45		
	MEDIAN	62.9		
	MIN, MAX	2.0, 571.6		
	5%, 95%	25.3, 194.1		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	87.2, 67.9		
	SD, SE	81.29, 11.50		
	MEDIAN	64.8		
	MIN, MAX	4.5, 538.8		
	5%, 95%	31.8, 161.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 42 of 264)

Biomarker: Cotinine ((nmol/L)/cigarette per day) Analytical Lab: Harrogate				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	422.4, 337.1		
	SD, SE	296.12, 41.88		
	MEDIAN	330.1		
	MIN, MAX	35.9, 1490.7		
	5%, 95%	85.7, 1070.4		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	557.6, 404.3		
	SD, SE	689.09, 98.44		
	MEDIAN	385.0		
	MIN, MAX	29.3, 4789.2		
	5%, 95%	168.0, 1355.9		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	515.3, 378.7		
	SD, SE	517.71, 76.33		
	MEDIAN	356.9		
	MIN, MAX	11.5, 3243.9		
	5%, 95%	143.8, 1101.4		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	494.9, 385.2		
	SD, SE	461.35, 65.24		
	MEDIAN	367.7		
	MIN, MAX	25.6, 3057.8		
	5%, 95%	180.6, 916.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 43 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/L)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	12245.232, 6153.631	7.692, NA	
	SD, SE	13823.3167, 1954.9122	18.2035, 2.2579	
	MEDIAN	6149.147	0.000	
	MIN, MAX	71.505, 58435.475	0.000, 121.445	
	5%, 95%	193.518, 44549.885	0.000, 38.023	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	14130.356, 7525.660	8.818, NA	
	SD, SE	15556.5168, 2222.3595	18.2860, 2.2681	
	MEDIAN	7567.613	1.135	
	MIN, MAX	73.775, 77152.193	0.000, 92.503	
	5%, 95%	310.423, 42263.995	0.000, 57.318	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	11201.759, 6697.690	5.553, NA	
	SD, SE	9178.1533, 1353.2449	12.2139, 1.5149	
	MEDIAN	8706.585	0.000	
	MIN, MAX	81.153, 37456.135	0.000, 78.883	
	5%, 95%	756.478, 27258.728	0.000, 22.700	
	# of BLQ/ALQ Values	0/0	50/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	12368.899, 7152.222	7.354, NA	
	SD, SE	11679.4403, 1651.7223	13.6122, 1.6884	
	MEDIAN	8028.612	0.946	
	MIN, MAX	75.478, 53864.641	0.000, 74.910	
	5%, 95%	430.165, 31626.019	0.000, 33.293	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 44 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	762.287, 472.703		
	SD, SE	771.9750, 109.1737		
	MEDIAN	527.289		
	MIN, MAX	23.835, 3712.490		
	5%, 95%	64.506, 2470.157		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	967.011, 607.184		
	SD, SE	899.6229, 128.5176		
	MEDIAN	591.851		
	MIN, MAX	24.592, 3857.610		
	5%, 95%	126.571, 2367.300		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	871.974, 533.895		
	SD, SE	863.9490, 127.3823		
	MEDIAN	578.252		
	MIN, MAX	27.051, 3961.718		
	5%, 95%	100.391, 2846.864		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	864.434, 571.783		
	SD, SE	729.4937, 103.1660		
	MEDIAN	698.097		
	MIN, MAX	25.159, 3026.032		
	5%, 95%	128.640, 2522.024		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 45 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	17584.204, 10515.717	12.227, NA	
	SD, SE	15317.1515, 2166.1723	25.2601, 3.1331	
	MEDIAN	13519.978	0.000	
	MIN, MAX	100.822, 68661.683	0.000, 106.872	
	5%, 95%	561.202, 52173.823	0.000, 75.621	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	18182.368, 11642.571	15.344, NA	
	SD, SE	14562.1275, 2080.3039	32.3372, 4.0109	
	MEDIAN	14973.828	1.396	
	MIN, MAX	66.398, 68665.452	0.000, 203.789	
	5%, 95%	523.023, 54491.407	0.000, 73.080	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	17809.284, 11430.892	9.953, NA	
	SD, SE	12417.3464, 1830.8378	21.2412, 2.6346	
	MEDIAN	16848.227	0.000	
	MIN, MAX	85.048, 48692.976	0.000, 105.328	
	5%, 95%	1043.940, 37176.403	0.000, 50.216	
	# of BLQ/ALQ Values	0/0	50/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	17588.204, 11451.596	12.508, NA	
	SD, SE	13197.5310, 1866.4127	22.7210, 2.8182	
	MEDIAN	15932.218	1.778	
	MIN, MAX	84.089, 57165.219	0.000, 104.966	
	5%, 95%	827.405, 46579.291	0.000, 50.161	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 46 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	1127.149, 807.784	
	SD, SE	1016.3918, 143.7395	
	MEDIAN	855.081	
	MIN, MAX	33.607, 6051.885	
	5%, 95%	142.017, 3069.048	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	1313.513, 939.344	
	SD, SE	1175.2250, 167.8893	
	MEDIAN	1020.252	
	MIN, MAX	22.133, 6205.773	
	5%, 95%	271.996, 3833.600	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	1270.167, 911.195	
	SD, SE	899.0178, 132.5529	
	MEDIAN	1086.509	
	MIN, MAX	28.349, 4080.569	
	5%, 95%	173.990, 3033.231	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	1232.649, 921.621	
	SD, SE	919.0081, 129.9674	
	MEDIAN	922.614	
	MIN, MAX	28.030, 5059.513	
	5%, 95%	249.511, 2716.257	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 47 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	13.335, 8.713	0.008, NA	
	SD, SE	9.4621, 1.3381	0.0174, 0.0022	
	MEDIAN	12.095	0.000	
	MIN, MAX	0.095, 37.108	0.000, 0.075	
	5%, 95%	0.507, 33.762	0.000, 0.055	
	# of BLQ/ALQ Values	0/0	49/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	13.437, 8.986	0.011, NA	
	SD, SE	10.4751, 1.4964	0.0269, 0.0033	
	MEDIAN	11.760	0.001	
	MIN, MAX	0.074, 53.877	0.000, 0.195	
	5%, 95%	0.522, 34.914	0.000, 0.043	
	# of BLQ/ALQ Values	0/0	47/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	13.808, 9.166	0.007, NA	
	SD, SE	10.2141, 1.5060	0.0144, 0.0018	
	MEDIAN	14.106	0.000	
	MIN, MAX	0.075, 49.743	0.000, 0.067	
	5%, 95%	1.668, 34.847	0.000, 0.035	
	# of BLQ/ALQ Values	0/0	50/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	13.481, 9.180	0.009, NA	
	SD, SE	9.5809, 1.3549	0.0167, 0.0021	
	MEDIAN	12.611	0.001	
	MIN, MAX	0.081, 38.906	0.000, 0.091	
	5%, 95%	0.809, 38.061	0.000, 0.047	

^a P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 48 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	NA
	MEAN, GEO MEAN	0.906, 0.670	
	SD, SE	0.7516, 0.1063	
	MEDIAN	0.648	
	MIN, MAX	0.032, 3.670	
	5%, 95%	0.169, 2.486	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	NA
	MEAN, GEO MEAN	1.052, 0.725	
	SD, SE	1.1509, 0.1644	
	MEDIAN	0.656	
	MIN, MAX	0.025, 6.653	
	5%, 95%	0.244, 2.843	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	NA
	MEAN, GEO MEAN	1.036, 0.731	
	SD, SE	0.9616, 0.1418	
	MEDIAN	0.754	
	MIN, MAX	0.025, 5.120	
	5%, 95%	0.209, 3.082	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	NA
	MEAN, GEO MEAN	1.004, 0.740	
	SD, SE	0.8814, 0.1246	
	MEDIAN	0.753	
	MIN, MAX	0.027, 4.364	
	5%, 95%	0.281, 2.594	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (µg/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1745.037, 1070.295	4.817, 2.136	
	SD, SE	1430.1976, 202.2605	13.3902, 1.6608	
	MEDIAN	1417.225	1.850	
	MIN, MAX	18.048, 5245.860	0.530, 93.100	
	5%, 95%	83.814, 4727.375	0.800, 13.992	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1806.112, 1170.199	7.050, 2.147	
	SD, SE	1358.1127, 194.0161	37.2887, 4.6251	
	MEDIAN	1573.750	2.000	
	MIN, MAX	10.980, 5904.527	0.625, 302.670	
	5%, 95%	94.792, 4729.200	0.815, 6.758	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	2033.500, 1264.500	2.387, 2.037	
	SD, SE	1625.9686, 239.7360	1.8384, 0.2280	
	MEDIAN	1632.768	2.000	
	MIN, MAX	5.450, 6614.080	0.750, 13.650	
	5%, 95%	161.699, 5668.540	0.990, 4.740	
	# of BLQ/ALQ Values	0/0	57/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	1827.982, 1226.585	4.751, 2.291	
	SD, SE	1277.8760, 180.7190	15.2674, 1.8937	
	MEDIAN	1696.911	2.143	
	MIN, MAX	11.493, 4824.558	0.793, 121.310	
	5%, 95%	130.092, 4297.933	0.980, 8.342	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 50 of 264)

Biomarker: Nicotine (nmol/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	10758.156, 6598.368	29.696, 13.171	
	SD, SE	8817.1680, 1246.9359	82.5504, 10.2391	
	MEDIAN	8737.192	11.405	
	MIN, MAX	111.266, 32340.727	3.267, 573.962	
	5%, 95%	516.713, 29144.267	4.932, 86.261	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	11134.681, 7214.277	43.463, 13.235	
	SD, SE	8372.7650, 1196.1093	229.8849, 28.5137	
	MEDIAN	9702.169	12.330	
	MIN, MAX	67.692, 36401.409	3.853, 1865.961	
	5%, 95%	584.393, 29155.518	5.024, 41.663	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	12536.527, 7795.640	14.714, 12.560	
	SD, SE	10024.0962, 1477.9724	11.3339, 1.4058	
	MEDIAN	10066.012	12.330	
	MIN, MAX	33.599, 40775.803	4.624, 84.152	
	5%, 95%	996.874, 34946.549	6.103, 29.222	
	# of BLQ/ALQ Values	0/0	57/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	11269.508, 7561.892	29.291, 14.125	
	SD, SE	7878.1057, 1114.1324	94.1236, 11.6746	
	MEDIAN	10461.455	13.214	
	MIN, MAX	70.852, 29743.402	4.891, 747.878	
	5%, 95%	802.013, 26496.759	6.042, 51.426	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 51 of 264)

Biomarker: Nicotine ((ug/24hr)/cigarette per day) Analytical Lab: Harrogate			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	116.774, 82.217	
	SD, SE	102.3062, 14.4683	
	MEDIAN	91.850	
	MIN, MAX	6.016, 590.746	
	5%, 95%	16.763, 272.020	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	153.863, 94.414	
	SD, SE	248.5400, 35.5057	
	MEDIAN	92.998	
	MIN, MAX	3.660, 1747.393	
	5%, 95%	16.394, 360.360	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	135.489, 100.798	
	SD, SE	90.2543, 13.3073	
	MEDIAN	121.820	
	MIN, MAX	1.817, 422.898	
	5%, 95%	23.100, 275.895	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	132.882, 100.253	
	SD, SE	123.8433, 17.5141	
	MEDIAN	116.709	
	MIN, MAX	3.831, 849.365	
	5%, 95%	39.378, 281.914	
			NA

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	719.909, 506.866		
	SD, SE	630.7173, 89.1969		
	MEDIAN	566.254		
	MIN, MAX	37.089, 3641.947		
	5%, 95%	103.343, 1677.003		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	948.567, 582.061		
	SD, SE	1532.2484, 218.8926		
	MEDIAN	573.331		
	MIN, MAX	22.564, 10772.675		
	5%, 95%	101.072, 2221.619		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	835.292, 621.417		
	SD, SE	556.4178, 82.0393		
	MEDIAN	751.016		
	MIN, MAX	11.200, 2607.168		
	5%, 95%	142.411, 1700.894		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	819.216, 618.061		
	SD, SE	763.4933, 107.9743		
	MEDIAN	719.512		
	MIN, MAX	23.618, 5236.332		
	5%, 95%	242.766, 1737.999		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (µg/mg Creatinine)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1.551, 0.887	0.003, NA	
	SD, SE	1.6269, 0.2301	0.0074, 0.0009	
	MEDIAN	1.072	0.001	
	MIN, MAX	0.017, 8.892	0.000, 0.044	
	5%, 95%	0.071, 5.001	0.000, 0.012	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1.459, 0.903	0.006, NA	
	SD, SE	1.3786, 0.1969	0.0357, 0.0044	
	MEDIAN	1.262	0.001	
	MIN, MAX	0.012, 6.916	0.000, 0.289	
	5%, 95%	0.071, 4.633	0.000, 0.004	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1.565, 1.015	0.002, NA	
	SD, SE	1.1600, 0.1710	0.0012, 0.0002	
	MEDIAN	1.471	0.001	
	MIN, MAX	0.005, 5.060	0.000, 0.008	
	5%, 95%	0.107, 4.177	0.000, 0.004	
	# of BLQ/ALQ Values	0/0	57/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	1.522, 0.990	0.004, NA	
	SD, SE	1.2602, 0.1782	0.0137, 0.0017	
	MEDIAN	1.351	0.002	
	MIN, MAX	0.011, 5.866	0.000, 0.111	
	5%, 95%	0.119, 4.066	0.001, 0.006	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 54 of 264)

Biomarker: Nicotine (nmol/mg Creatinine)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	9.559, 5.466	0.020, NA	
	SD, SE	10.0298, 1.4184	0.0459, 0.0057	
	MEDIAN	6.606	0.006	
	MIN, MAX	0.105, 54.819	0.000, 0.271	
	5%, 95%	0.438, 30.831	0.000, 0.074	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	8.998, 5.566	0.039, NA	
	SD, SE	8.4990, 1.2141	0.2199, 0.0273	
	MEDIAN	7.780	0.006	
	MIN, MAX	0.074, 42.637	0.000, 1.782	
	5%, 95%	0.438, 28.562	0.000, 0.025	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	9.650, 6.259	0.010, NA	
	SD, SE	7.1517, 1.0545	0.0076, 0.0009	
	MEDIAN	9.066	0.006	
	MIN, MAX	0.031, 31.195	0.000, 0.049	
	5%, 95%	0.660, 25.751	0.000, 0.025	
	# of BLQ/ALQ Values	0/0	57/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	9.382, 6.109	0.023, NA	
	SD, SE	7.7691, 1.0987	0.0841, 0.0104	
	MEDIAN	8.328	0.010	
	MIN, MAX	0.070, 36.164	0.000, 0.682	
	5%, 95%	0.734, 25.067	0.004, 0.039	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 55 of 264)

Biomarker: Nicotine ((μ g/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	0.121, 0.068		
	SD, SE	0.2468, 0.0349		
	MEDIAN	0.071		
	MIN, MAX	0.006, 1.778		
	5%, 95%	0.014, 0.191		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.161, 0.073		
	SD, SE	0.4856, 0.0694		
	MEDIAN	0.065		
	MIN, MAX	0.004, 3.458		
	5%, 95%	0.013, 0.244		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.110, 0.081		
	SD, SE	0.0761, 0.0112		
	MEDIAN	0.091		
	MIN, MAX	0.002, 0.358		
	5%, 95%	0.016, 0.255		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	0.130, 0.081		
	SD, SE	0.2565, 0.0363		
	MEDIAN	0.081		
	MIN, MAX	0.004, 1.865		
	5%, 95%	0.023, 0.227		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	0.747, 0.420	
	SD, SE	1.5220, 0.2152	
	MEDIAN	0.438	
	MIN, MAX	0.035, 10.964	
	5%, 95%	0.088, 1.178	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	0.991, 0.449	
	SD, SE	2.9937, 0.4277	
	MEDIAN	0.400	
	MIN, MAX	0.025, 21.319	
	5%, 95%	0.079, 1.504	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	0.675, 0.499	
	SD, SE	0.4695, 0.0692	
	MEDIAN	0.564	
	MIN, MAX	0.010, 2.207	
	5%, 95%	0.099, 1.570	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	0.800, 0.500	
	SD, SE	1.5812, 0.2236	
	MEDIAN	0.499	
	MIN, MAX	0.023, 11.497	
	5%, 95%	0.143, 1.399	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (ng/mL)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1141.8, 626.3	2.2, 1.3	
	SD, SE	1210.89, 171.25	4.25, 0.53	
	MEDIAN	649.3	1.0	
	MIN, MAX	12.8, 6329.6	1.0, 24.5	
	5%, 95%	45.8, 3752.0	1.0, 6.8	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1245.5, 756.4	2.9, 1.3	
	SD, SE	1251.38, 178.77	13.05, 1.62	
	MEDIAN	835.4	1.0	
	MIN, MAX	12.2, 6634.3	1.0, 106.2	
	5%, 95%	83.5, 3489.6	1.0, 4.3	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1166.7, 740.9	1.2, 1.1	
	SD, SE	933.84, 137.69	1.24, 0.15	
	MEDIAN	911.3	1.0	
	MIN, MAX	5.2, 3630.2	1.0, 10.5	
	5%, 95%	131.0, 3006.4	1.0, 1.7	
	# of BLQ/ALQ Values	0/0	57/0	
Overall [*]	N	50	65	<.0001
	MEAN, GEO MEAN	1167.2, 745.0	2.1, 1.3	
	SD, SE	1017.73, 143.93	5.34, 0.66	
	MEDIAN	815.5	1.0	
	MIN, MAX	10.1, 5531.4	1.0, 42.7	
	5%, 95%	69.4, 2950.7	1.0, 3.3	

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (nmol/L)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	7039.3, 3861.3	13.5, 8.1	
	SD, SE	7465.15, 1055.73	26.18, 3.25	
	MEDIAN	4002.7	6.2	
	MIN, MAX	78.9, 39022.0	6.2, 151.0	
	5%, 95%	282.4, 23131.1	6.2, 41.9	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	7678.6, 4663.2	18.2, 7.7	
	SD, SE	7714.75, 1102.11	80.42, 9.97	
	MEDIAN	5150.2	6.2	
	MIN, MAX	75.2, 40900.5	6.2, 654.7	
	5%, 95%	514.8, 21513.4	6.2, 26.5	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	7192.6, 4567.8	7.6, 6.8	
	SD, SE	5757.14, 848.84	7.61, 0.94	
	MEDIAN	5618.2	6.2	
	MIN, MAX	32.1, 22380.2	6.2, 64.7	
	5%, 95%	807.6, 18534.5	6.2, 10.5	
	# of BLQ/ALQ Values	0/0	57/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	7196.0, 4592.7	13.1, 8.1	
	SD, SE	6274.31, 887.32	32.91, 4.08	
	MEDIAN	5027.4	6.2	
	MIN, MAX	62.1, 34100.9	6.2, 263.2	
	5%, 95%	427.6, 18191.3	6.2, 20.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	74.5, 48.1	
	SD, SE	73.23, 10.36	
	MEDIAN	53.8	
	MIN, MAX	4.3, 312.7	
	5%, 95%	9.2, 287.7	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	103.7, 61.0	
	SD, SE	166.97, 23.85	
	MEDIAN	55.7	
	MIN, MAX	4.1, 1127.4	
	5%, 95%	15.7, 307.9	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	85.9, 59.0	
	SD, SE	76.09, 11.22	
	MEDIAN	66.1	
	MIN, MAX	1.7, 374.9	
	5%, 95%	14.7, 242.0	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	86.4, 60.6	
	SD, SE	93.76, 13.26	
	MEDIAN	55.0	
	MIN, MAX	3.4, 603.3	
	5%, 95%	20.1, 210.8	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((nmol/L)/cigarette per day) Analytical Lab: Harrogate			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	459.0, 296.6	
	SD, SE	451.47, 63.85	
	MEDIAN	331.6	
	MIN, MAX	26.3, 1927.6	
	5%, 95%	56.5, 1773.7	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	639.3, 376.3	
	SD, SE	1029.33, 147.05	
	MEDIAN	343.3	
	MIN, MAX	25.1, 6950.1	
	5%, 95%	97.0, 1898.3	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	529.4, 364.1	
	SD, SE	469.06, 69.16	
	MEDIAN	407.3	
	MIN, MAX	10.7, 2311.4	
	5%, 95%	90.3, 1492.0	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	532.9, 373.4	
	SD, SE	578.08, 81.75	
	MEDIAN	339.1	
	MIN, MAX	20.7, 3719.4	
	5%, 95%	123.7, 1299.5	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide (nmol/L)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	62	<.0001
	MEAN, GEO MEAN	2978.211, 1359.261	1.810, NA	
	SD, SE	3802.1449, 543.1636	4.2784, 0.5434	
	MEDIAN	1405.004	0.000	
	MIN, MAX	17.879, 17624.502	0.000, 22.811	
	5%, 95%	71.514, 11547.045	0.000, 9.248	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	48	63	<.0001
	MEAN, GEO MEAN	3456.562, 1750.146	2.593, NA	
	SD, SE	4353.5928, 628.3870	12.6584, 1.5948	
	MEDIAN	1479.292	0.000	
	MIN, MAX	68.432, 25269.102	0.000, 99.257	
	5%, 95%	121.451, 10055.115	0.000, 9.864	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	45	65	<.0001
	MEAN, GEO MEAN	2802.102, 1441.503	1.328, NA	
	SD, SE	2424.2917, 361.3921	4.0898, 0.5073	
	MEDIAN	2594.232	0.000	
	MIN, MAX	12.330, 8494.754	0.000, 28.976	
	5%, 95%	27.126, 8015.733	0.000, 6.165	
	# of BLQ/ALQ Values	0/0	57/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	2971.557, 1586.553	1.914, NA	
	SD, SE	3164.2230, 447.4887	5.4016, 0.6700	
	MEDIAN	1558.718	0.000	
	MIN, MAX	22.503, 14522.685	0.000, 36.579	
	5%, 95%	98.640, 9135.914	0.000, 7.707	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	186.474, 106.209		
	SD, SE	226.2210, 32.3173		
	MEDIAN	100.816		
	MIN, MAX	5.960, 1036.735		
	5%, 95%	18.187, 720.449		
	# of BLQ/ALQ Values	0/0		
Week 2	N	48		NA
	MEAN, GEO MEAN	237.481, 137.093		
	SD, SE	267.3848, 38.5937		
	MEDIAN	139.734		
	MIN, MAX	4.562, 1263.455		
	5%, 95%	33.044, 730.384		
	# of BLQ/ALQ Values	0/0		
Week 3	N	45		NA
	MEAN, GEO MEAN	213.931, 113.039		
	SD, SE	198.0646, 29.5257		
	MEDIAN	145.682		
	MIN, MAX	1.192, 674.143		
	5%, 95%	9.042, 555.261		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	206.210, 127.824		
	SD, SE	200.0369, 28.2895		
	MEDIAN	126.274		
	MIN, MAX	7.501, 756.966		
	5%, 95%	25.616, 705.631		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide (nmol/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	49	62	<.0001
	MEAN, GEO MEAN	4098.496, 2293.981	3.042, NA	
	SD, SE	4073.6525, 581.9504	7.0213, 0.8917	
	MEDIAN	2740.959	0.000	
	MIN, MAX	25.209, 22030.628	0.000, 29.594	
	5%, 95%	162.756, 10788.304	0.000, 22.042	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	48	63	<.0001
	MEAN, GEO MEAN	4409.210, 2738.292	6.347, NA	
	SD, SE	4279.9893, 617.7632	35.7513, 4.5042	
	MEDIAN	3529.189	0.000	
	MIN, MAX	177.318, 22489.501	0.000, 282.882	
	5%, 95%	294.258, 11807.486	0.000, 14.886	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	45	65	<.0001
	MEAN, GEO MEAN	4437.910, 2471.845	2.326, NA	
	SD, SE	3364.7124, 501.5817	6.2367, 0.7736	
	MEDIAN	4005.325	0.000	
	MIN, MAX	17.262, 12487.288	0.000, 37.669	
	5%, 95%	52.296, 10485.827	0.000, 14.303	
	# of BLQ/ALQ Values	0/0	57/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	4172.890, 2585.250	3.898, NA	
	SD, SE	3505.6233, 495.7700	13.5723, 1.6834	
	MEDIAN	3084.908	0.000	
	MIN, MAX	26.819, 15441.801	0.000, 104.041	
	5%, 95%	199.791, 11219.242	0.000, 18.618	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	266.383, 179.244		
	SD, SE	263.2107, 37.6015		
	MEDIAN	183.997		
	MIN, MAX	8.403, 1295.919		
	5%, 95%	24.734, 837.161		
	# of BLQ/ALQ Values	0/0		
Week 2	N	48		NA
	MEAN, GEO MEAN	325.513, 214.496		
	SD, SE	356.1870, 51.4112		
	MEDIAN	200.027		
	MIN, MAX	19.617, 1880.171		
	5%, 95%	59.810, 1124.475		
	# of BLQ/ALQ Values	0/0		
Week 3	N	45		NA
	MEAN, GEO MEAN	317.537, 193.835		
	SD, SE	251.3426, 37.4679		
	MEDIAN	253.798		
	MIN, MAX	3.452, 929.600		
	5%, 95%	9.476, 741.273		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	295.119, 209.508		
	SD, SE	251.5093, 35.5688		
	MEDIAN	189.633		
	MIN, MAX	8.940, 1230.708		
	5%, 95%	43.896, 767.442		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 65 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	49	62	<.0001
	MEAN, GEO MEAN	3.019, 1.886	0.002, NA	
	SD, SE	2.3754, 0.3393	0.0048, 0.0006	
	MEDIAN	2.774	0.000	
	MIN, MAX	0.024, 12.113	0.000, 0.023	
	5%, 95%	0.135, 7.058	0.000, 0.012	
	# of BLQ/ALQ Values	0/0	51/0	
Week 2	N	48	63	<.0001
	MEAN, GEO MEAN	3.238, 2.097	0.006, NA	
	SD, SE	3.1048, 0.4481	0.0340, 0.0043	
	MEDIAN	2.471	0.000	
	MIN, MAX	0.153, 17.646	0.000, 0.270	
	5%, 95%	0.222, 6.805	0.000, 0.011	
	# of BLQ/ALQ Values	0/0	54/0	
Week 3	N	45	65	<.0001
	MEAN, GEO MEAN	3.372, 1.946	0.001, NA	
	SD, SE	2.5882, 0.3858	0.0034, 0.0004	
	MEDIAN	2.840	0.000	
	MIN, MAX	0.020, 10.645	0.000, 0.021	
	5%, 95%	0.056, 8.031	0.000, 0.008	
	# of BLQ/ALQ Values	0/0	57/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	3.169, 2.071	0.003, NA	
	SD, SE	2.4360, 0.3445	0.0122, 0.0015	
	MEDIAN	2.648	0.000	
	MIN, MAX	0.025, 10.339	0.000, 0.097	
	5%, 95%	0.190, 8.383	0.000, 0.009	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	49	
	MEAN, GEO MEAN	0.209, 0.147	
	SD, SE	0.1807, 0.0258	
	MEDIAN	0.139	
	MIN, MAX	0.008, 0.713	
	5%, 95%	0.031, 0.679	
	# of BLQ/ALQ Values	0/0	
Week 2	N	48	
	MEAN, GEO MEAN	0.258, 0.164	
	SD, SE	0.3189, 0.0460	
	MEDIAN	0.151	
	MIN, MAX	0.015, 1.647	
	5%, 95%	0.051, 0.882	
	# of BLQ/ALQ Values	0/0	
Week 3	N	45	
	MEAN, GEO MEAN	0.251, 0.153	
	SD, SE	0.2391, 0.0356	
	MEDIAN	0.165	
	MIN, MAX	0.004, 1.213	
	5%, 95%	0.008, 0.710	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	0.237, 0.168	
	SD, SE	0.2165, 0.0306	
	MEDIAN	0.150	
	MIN, MAX	0.008, 1.065	
	5%, 95%	0.042, 0.590	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 67 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	68.467, 49.888	0.073, NA	
	SD, SE	43.2595, 6.1178	0.1188, 0.0147	
	MEDIAN	62.776	0.033	
	MIN, MAX	0.762, 171.322	0.000, 0.677	
	5%, 95%	8.068, 162.785	0.017, 0.340	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	69.207, 51.472	0.112, NA	
	SD, SE	45.1471, 6.4496	0.3667, 0.0455	
	MEDIAN	63.557	0.033	
	MIN, MAX	0.520, 177.245	0.000, 2.938	
	5%, 95%	10.256, 162.182	0.016, 0.209	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	71.913, 53.378	0.057, 0.039	
	SD, SE	46.2520, 6.8195	0.0733, 0.0091	
	MEDIAN	62.122	0.033	
	MIN, MAX	0.402, 204.112	0.011, 0.470	
	5%, 95%	14.475, 163.660	0.017, 0.174	
	# of BLQ/ALQ Values	0/0	0/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	69.731, 52.459	0.081, 0.044	
	SD, SE	43.5014, 6.1520	0.1621, 0.0201	
	MEDIAN	64.514	0.035	
	MIN, MAX	0.561, 182.343	0.011, 1.222	
	5%, 95%	10.933, 150.824	0.017, 0.255	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	4.963, 3.832	
	SD, SE	4.9765, 0.7038	
	MEDIAN	3.716	
	MIN, MAX	0.254, 34.264	
	5%, 95%	1.063, 12.963	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	6.263, 4.133	
	SD, SE	11.2861, 1.6123	
	MEDIAN	3.606	
	MIN, MAX	0.173, 81.091	
	5%, 95%	1.734, 11.330	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	5.325, 4.255	
	SD, SE	4.1846, 0.6170	
	MEDIAN	4.197	
	MIN, MAX	0.134, 23.794	
	5%, 95%	1.911, 10.156	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	5.541, 4.232	
	SD, SE	6.4550, 0.9129	
	MEDIAN	4.068	
	MIN, MAX	0.187, 46.383	
	5%, 95%	1.877, 11.763	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/24hr)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	13.490, 9.768	0.017, 0.009	
	SD, SE	8.8670, 1.2540	0.0302, 0.0037	
	MEDIAN	13.234	0.007	
	MIN, MAX	0.131, 43.641	0.002, 0.157	
	5%, 95%	2.343, 27.701	0.003, 0.063	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	14.364, 10.818	0.024, 0.010	
	SD, SE	8.3444, 1.1921	0.0652, 0.0081	
	MEDIAN	14.064	0.008	
	MIN, MAX	0.075, 36.320	0.002, 0.499	
	5%, 95%	2.125, 33.028	0.003, 0.056	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	14.587, 10.799	0.014, 0.009	
	SD, SE	8.9934, 1.3260	0.0208, 0.0026	
	MEDIAN	13.707	0.007	
	MIN, MAX	0.074, 41.355	0.003, 0.136	
	5%, 95%	2.138, 32.720	0.004, 0.060	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	13.934, 10.577	0.018, 0.010	
	SD, SE	8.1211, 1.1485	0.0336, 0.0042	
	MEDIAN	13.706	0.008	
	MIN, MAX	0.093, 37.247	0.003, 0.222	
	5%, 95%	2.359, 27.579	0.003, 0.065	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/24hr)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	0.898, 0.750	
	SD, SE	0.5491, 0.0777	
	MEDIAN	0.786	
	MIN, MAX	0.044, 3.468	
	5%, 95%	0.273, 1.684	
Week 2	# of BLQ/ALQ Values	0/0	
	N	49	
	MEAN, GEO MEAN	1.118, 0.873	
	SD, SE	1.0211, 0.1459	
	MEDIAN	0.868	
	MIN, MAX	0.025, 6.647	
Week 3	5%, 95%	0.425, 2.761	
	# of BLQ/ALQ Values	0/0	
	N	46	
	MEAN, GEO MEAN	1.023, 0.861	
	SD, SE	0.5242, 0.0773	
	MEDIAN	0.982	
Overall*	MIN, MAX	0.025, 2.263	
	5%, 95%	0.420, 2.083	
	# of BLQ/ALQ Values	0/0	
	N	50	
	MEAN, GEO MEAN	1.008, 0.852	
	SD, SE	0.6034, 0.0853	
Overall*	MEDIAN	0.955	
	MIN, MAX	0.031, 3.585	
	5%, 95%	0.402, 1.810	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/mg Creatinine)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	0.011, NA	0.000, NA	
	SD, SE	0.0071, 0.0010	0.0000, 0.0000	
	MEDIAN	0.010	0.000	
	MIN, MAX	0.000, 0.028	0.000, 0.000	
	5%, 95%	0.001, 0.026	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	0.011, NA	0.000, NA	
	SD, SE	0.0073, 0.0010	0.0000, 0.0000	
	MEDIAN	0.010	0.000	
	MIN, MAX	0.000, 0.029	0.000, 0.000	
	5%, 95%	0.002, 0.026	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	0.012, NA	0.000, NA	
	SD, SE	0.0075, 0.0011	0.0000, 0.0000	
	MEDIAN	0.010	0.000	
	MIN, MAX	0.000, 0.033	0.000, 0.000	
	5%, 95%	0.002, 0.027	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	0.011, NA	0.000, NA	
	SD, SE	0.0071, 0.0010	0.0000, 0.0000	
	MEDIAN	0.010	0.000	
	MIN, MAX	0.000, 0.030	0.000, 0.000	
	5%, 95%	0.002, 0.024	0.000, 0.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0009, 0.0001		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.006		
	5%, 95%	0.000, 0.002		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0019, 0.0003		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.013		
	5%, 95%	0.000, 0.002		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0007, 0.0001		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.004		
	5%, 95%	0.000, 0.002		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0012, 0.0002		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.008		
	5%, 95%	0.000, 0.002		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/24hr)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	83153.584, 60208.430	105.530, 54.081	
	SD, SE	54657.1229, 7729.6845	186.1554, 23.0897	
	MEDIAN	81571.855	44.994	
	MIN, MAX	807.495, 269008.088	13.634, 965.245	
	5%, 95%	14441.244, 170748.968	17.554, 388.382	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	88539.575, 66686.156	145.907, 62.366	
	SD, SE	51435.3073, 7347.9010	401.7923, 49.8362	
	MEDIAN	86689.522	49.426	
	MIN, MAX	463.520, 223877.537	12.603, 3077.553	
	5%, 95%	13096.445, 203586.824	17.436, 344.801	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	89914.281, 66565.555	85.407, 54.691	
	SD, SE	55436.2027, 8173.6222	128.0726, 15.8854	
	MEDIAN	84489.955	45.164	
	MIN, MAX	455.443, 254916.322	17.387, 838.565	
	5%, 95%	13178.209, 201686.943	22.786, 368.107	
	# of BLQ/ALQ Values	0/0	0/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	85889.343, 65200.410	112.281, 61.187	
	SD, SE	50059.2543, 7079.4476	207.3678, 25.7208	
	MEDIAN	84481.890	48.290	
	MIN, MAX	575.486, 229597.547	16.995, 1369.102	
	5%, 95%	14539.033, 169998.026	21.248, 401.405	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 74 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50		NA
	MEAN, GEO MEAN	5533.031, 4625.021		
	SD, SE	3384.8254, 478.6866		
	MEDIAN	4847.574		
	MIN, MAX	269.165, 21374.817		
	5%, 95%	1679.783, 10379.541		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	6892.223, 5380.358		
	SD, SE	6294.2825, 899.1832		
	MEDIAN	5348.991		
	MIN, MAX	154.507, 40974.206		
	5%, 95%	2619.289, 17016.199		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	6307.558, 5306.163		
	SD, SE	3231.3395, 476.4350		
	MEDIAN	6055.057		
	MIN, MAX	151.814, 13950.879		
	5%, 95%	2586.936, 12841.396		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	6214.769, 5252.453		
	SD, SE	3719.8748, 526.0697		
	MEDIAN	5888.948		
	MIN, MAX	191.829, 22102.107		
	5%, 95%	2475.432, 11156.032		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/L)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	53238.5, 35233.1	60.0, 33.2	
	SD, SE	44982.55, 6361.49	113.33, 14.06	
	MEDIAN	40007.4	22.9	
	MIN, MAX	572.7, 228943.1	17.1, 822.3	
	5%, 95%	5370.5, 128475.6	17.1, 184.7	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	62854.0, 43105.3	80.2, 36.4	
	SD, SE	51855.77, 7407.97	187.75, 23.29	
	MEDIAN	51484.6	23.5	
	MIN, MAX	515.0, 251547.8	17.1, 1079.8	
	5%, 95%	10010.5, 175038.6	17.1, 202.6	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	53561.0, 39002.7	45.9, 29.4	
	SD, SE	36385.03, 5364.68	82.65, 10.25	
	MEDIAN	45888.2	19.7	
	MIN, MAX	434.6, 161187.4	17.1, 645.0	
	5%, 95%	9549.4, 124561.5	17.1, 129.4	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	55931.5, 40417.7	62.1, 35.5	
	SD, SE	39513.50, 5588.05	105.04, 13.03	
	MEDIAN	44451.7	25.8	
	MIN, MAX	507.4, 177780.1	17.1, 555.8	
	5%, 95%	8324.0, 129505.1	17.1, 238.2	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234³ will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	3482.0, 2706.5		
	SD, SE	2373.66, 335.69		
	MEDIAN	2775.4		
	MIN, MAX	190.9, 10706.3		
	5%, 95%	879.4, 8428.7		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	4789.0, 3477.8		
	SD, SE	4453.70, 636.24		
	MEDIAN	3777.3		
	MIN, MAX	171.7, 26435.0		
	5%, 95%	1287.1, 13281.7		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	4222.5, 3109.1		
	SD, SE	4026.79, 593.72		
	MEDIAN	3189.7		
	MIN, MAX	144.9, 24912.3		
	5%, 95%	1250.6, 11279.6		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	4157.8, 3236.2		
	SD, SE	3182.56, 450.08		
	MEDIAN	3658.4		
	MIN, MAX	169.2, 19091.7		
	5%, 95%	1248.9, 9143.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 77 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/L) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	8.6, 5.7	0.0, NA	
	SD, SE	7.30, 1.03	0.02, 0.00	
	MEDIAN	6.5	0.0	
	MIN, MAX	0.1, 37.1	0.0, 0.1	
	5%, 95%	0.9, 20.8	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	10.2, 7.0	0.0, NA	
	SD, SE	8.41, 1.20	0.04, 0.00	
	MEDIAN	8.4	0.0	
	MIN, MAX	0.1, 40.8	0.0, 0.2	
	5%, 95%	1.6, 28.4	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	8.7, 6.4	0.0, NA	
	SD, SE	5.90, 0.87	0.01, 0.00	
	MEDIAN	7.5	0.0	
	MIN, MAX	0.1, 26.1	0.0, 0.1	
	5%, 95%	1.5, 20.2	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	9.1, 6.6	0.0, NA	
	SD, SE	6.41, 0.91	0.02, 0.00	
	MEDIAN	7.2	0.0	
	MIN, MAX	0.1, 28.8	0.0, 0.1	
	5%, 95%	1.4, 21.0	0.0, 0.0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 78 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/L)/cigarette per day)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50		NA
	MEAN, GEO MEAN	0.6, NA		
	SD, SE	0.39, 0.05		
	MEDIAN	0.5		
	MIN, MAX	0.0, 1.7		
	5%, 95%	0.1, 1.4		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.8, NA		
	SD, SE	0.73, 0.10		
	MEDIAN	0.6		
	MIN, MAX	0.0, 4.3		
	5%, 95%	0.2, 2.2		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.7, NA		
	SD, SE	0.65, 0.10		
	MEDIAN	0.6		
	MIN, MAX	0.0, 4.0		
	5%, 95%	0.2, 1.8		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	0.7, NA		
	SD, SE	0.52, 0.07		
	MEDIAN	0.6		
	MIN, MAX	0.0, 3.1		
	5%, 95%	0.2, 1.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 79 of 264)

Biomarker: Total 3-hydroxycotinine (µg/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	7831.126, 5355.823	8.345, 3.989	
	SD, SE	6001.9523, 848.8042	14.4819, 1.7963	
	MEDIAN	7518.912	3.000	
	MIN, MAX	80.370, 31233.615	0.800, 84.568	
	5%, 95%	795.900, 18631.252	1.140, 40.870	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	8569.600, 6203.499	11.570, 4.793	
	SD, SE	5412.4118, 773.2017	26.0279, 3.2284	
	MEDIAN	7610.064	3.150	
	MIN, MAX	48.420, 22147.192	1.000, 191.422	
	5%, 95%	842.508, 19677.560	1.148, 43.240	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	8483.711, 5938.857	7.990, 4.094	
	SD, SE	6120.1667, 902.3694	14.5318, 1.8024	
	MEDIAN	6586.053	3.219	
	MIN, MAX	52.295, 27454.900	1.068, 89.830	
	5%, 95%	1258.180, 18489.870	1.350, 44.835	
	# of BLQ/ALQ Values	0/0	25/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	8179.595, 5975.973	9.301, 4.690	
	SD, SE	5444.3965, 769.9539	16.0740, 1.9937	
	MEDIAN	6813.151	3.309	
	MIN, MAX	60.362, 23472.750	1.067, 97.065	
	5%, 95%	827.503, 20711.634	1.353, 42.982	

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/24hr) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	40745.351, 27866.345	43,416, 20,752	
	SD, SE	31228.1578, 4416.3284	75,3495, 9,3459	
	MEDIAN	39120.900	15,609	
	MIN, MAX	418.165, 162508.499	4,162, 440,007	
	5%, 95%	4141.068, 96938.404	5,931, 212,647	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	44587.629, 32276.804	60,197, 24,940	
	SD, SE	28160.7785, 4022.9684	135,4230, 16,7972	
	MEDIAN	39595.163	16,389	
	MIN, MAX	251,929, 115231.840	5,203, 995,969	
	5%, 95%	4383.569, 102382.345	5,973, 224,978	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	44140.746, 30899.874	41,570, 21,301	
	SD, SE	31843.2274, 4695.0277	75,6090, 9,3781	
	MEDIAN	34267.231	16,748	
	MIN, MAX	272,091, 142847.845	5,557, 467,385	
	5%, 95%	6546.311, 96202.794	7,024, 233,277	
	# of BLQ/ALQ Values	0/0	25/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	42558.433, 31092.983	48,394, 24,402	
	SD, SE	28327.1955, 4006.0704	83,6332, 10,3734	
	MEDIAN	35448.825	17,217	
	MIN, MAX	314,062, 122128.717	5,550, 505,029	
	5%, 95%	4305.496, 107762.632	7,048, 223,634	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((ug/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	515.834, 411.417		
	SD, SE	327.1857, 46.2710		
	MEDIAN	470.075		
	MIN, MAX	26.790, 1738.618		
	5%, 95%	92.813, 1160.539		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	658.768, 500.509		
	SD, SE	565.0482, 80.7212		
	MEDIAN	529.433		
	MIN, MAX	16.140, 3571.898		
	5%, 95%	226.150, 1632.510		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	592.291, 473.406		
	SD, SE	368.0561, 54.2669		
	MEDIAN	506.162		
	MIN, MAX	17.432, 1676.349		
	5%, 95%	222.522, 1418.901		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	588.904, 478.775		
	SD, SE	363.6626, 51.4297		
	MEDIAN	499.268		
	MIN, MAX	20.121, 2030.196		
	5%, 95%	199.073, 1303.658		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	2683.886, 2140.604		
	SD, SE	1702.3472, 240.7483		
	MEDIAN	2445.801		
	MIN, MAX	139.388, 9046.030		
	5%, 95%	482.904, 6038.287		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	3427.569, 2604.150		
	SD, SE	2939.9458, 419.9923		
	MEDIAN	2754.642		
	MIN, MAX	83.976, 18584.583		
	5%, 95%	1176.658, 8493.950		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	3081.692, 2463.133		
	SD, SE	1914.9958, 282.3507		
	MEDIAN	2633.560		
	MIN, MAX	90.697, 8722.043		
	5%, 95%	1157.784, 7382.540		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	3064.067, 2491.068		
	SD, SE	1892.1364, 267.5885		
	MEDIAN	2597.689		
	MIN, MAX	104.687, 10563.111		
	5%, 95%	1035.779, 6782.931		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	6.449, 4.438	0.006, NA	
	SD, SE	4.6629, 0.6594	0.0098, 0.0012	
	MEDIAN	5.375	0.002	
	MIN, MAX	0.076, 18.383	0.000, 0.052	
	5%, 95%	0.370, 15.997	0.001, 0.022	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	6.772, 4.788	0.008, NA	
	SD, SE	4.9259, 0.7037	0.0156, 0.0019	
	MEDIAN	5.554	0.002	
	MIN, MAX	0.054, 20.024	0.000, 0.099	
	5%, 95%	0.503, 18.134	0.001, 0.027	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	6.924, 4.762	0.005, 0.003	
	SD, SE	5.3191, 0.7843	0.0080, 0.0010	
	MEDIAN	5.015	0.002	
	MIN, MAX	0.046, 23.294	0.001, 0.050	
	5%, 95%	1.148, 17.524	0.001, 0.021	
	# of BLQ/ALQ Values	0/0	25/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	6.692, 4.787	0.006, 0.003	
	SD, SE	4.8008, 0.6789	0.0095, 0.0012	
	MEDIAN	5.297	0.003	
	MIN, MAX	0.039, 20.195	0.001, 0.046	
	5%, 95%	0.653, 16.414	0.001, 0.026	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	33.556, 23.089	0.030, NA	
	SD, SE	24.2611, 3.4310	0.0509, 0.0063	
	MEDIAN	27.964	0.010	
	MIN, MAX	0.395, 95.647	0.000, 0.271	
	5%, 95%	1.925, 83.232	0.005, 0.114	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	35.235, 24.911	0.040, NA	
	SD, SE	25.6293, 3.6613	0.0811, 0.0101	
	MEDIAN	28.897	0.010	
	MIN, MAX	0.281, 104.185	0.000, 0.515	
	5%, 95%	2.617, 94.331	0.005, 0.140	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	36.028, 24.775	0.026, 0.015	
	SD, SE	27.6752, 4.0805	0.0415, 0.0051	
	MEDIAN	26.091	0.010	
	MIN, MAX	0.239, 121.199	0.005, 0.260	
	5%, 95%	5.973, 91.177	0.005, 0.109	
	# of BLQ/ALQ Values	0/0	25/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	34.818, 24.906	0.032, 0.017	
	SD, SE	24.9784, 3.5325	0.0493, 0.0061	
	MEDIAN	27.557	0.016	
	MIN, MAX	0.305, 105.075	0.003, 0.241	
	5%, 95%	3.399, 85.402	0.005, 0.135	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 85 of 264)

Biomarker: Total 3-hydroxycotinine (ug/mg Creatinine/Cigarette per day) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50		NA
	MEAN, GEO MEAN	0.457, 0.341		
	SD, SE	0.4171, 0.0590		
	MEDIAN	0.376		
	MIN, MAX	0.021, 2.536		
	5%, 95%	0.077, 1.054		
Week 2	# of BLQ/ALQ Values	0/0		NA
	N	49		
	MEAN, GEO MEAN	0.595, 0.386		
	SD, SE	0.9893, 0.1413		
	MEDIAN	0.377		
	MIN, MAX	0.018, 7.069		
Week 3	5%, 95%	0.139, 1.211		NA
	# of BLQ/ALQ Values	0/0		
	N	46		
	MEAN, GEO MEAN	0.511, 0.380		
	SD, SE	0.4645, 0.0685		
	MEDIAN	0.381		
Overall ^b	MIN, MAX	0.015, 2.859		NA
	5%, 95%	0.151, 1.165		
	# of BLQ/ALQ Values	0/0		
	N	50		
	MEAN, GEO MEAN	0.524, 0.384		
	SD, SE	0.5899, 0.0834		
	MEDIAN	0.406		
	MIN, MAX	0.019, 4.155		
	5%, 95%	0.163, 1.346		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 86 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/mg Creatinine/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	2.376, 1.774		
	SD, SE	2.1705, 0.3070		
	MEDIAN	1.956		
	MIN, MAX	0.107, 13.195		
	5%, 95%	0.401, 5.486		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	3.097, 2.010		
	SD, SE	5.1472, 0.7353		
	MEDIAN	1.964		
	MIN, MAX	0.094, 36.780		
	5%, 95%	0.725, 6.299		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	2.659, 1.975		
	SD, SE	2.4170, 0.3564		
	MEDIAN	1.981		
	MIN, MAX	0.080, 14.876		
	5%, 95%	0.786, 6.061		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	2.726, 1.999		
	SD, SE	3.0691, 0.4340		
	MEDIAN	2.113		
	MIN, MAX	0.102, 21.617		
	5%, 95%	0.850, 7.002		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (ng/mL)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	4845.2, 3134.1	5.3, 2.4	
	SD, SE	4478.12, 633.30	12.40, 1.54	
	MEDIAN	3846.4	1.5	
	MIN, MAX	57.0, 26581.8	1.0, 96.1	
	5%, 95%	547.1, 12291.4	1.0, 18.0	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	5978.4, 4009.9	7.7, 2.8	
	SD, SE	4841.56, 691.65	22.20, 2.75	
	MEDIAN	4802.7	2.0	
	MIN, MAX	53.8, 23327.3	1.0, 169.4	
	5%, 95%	807.0, 16284.7	1.0, 26.2	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	5051.2, 3479.7	4.4, 2.2	
	SD, SE	4249.51, 626.56	9.19, 1.14	
	MEDIAN	4050.7	1.4	
	MIN, MAX	49.9, 23404.7	1.0, 69.1	
	5%, 95%	703.4, 12479.5	1.0, 15.6	
	# of BLQ/ALQ Values	0/0	25/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	5246.8, 3729.5	5.8, 2.7	
	SD, SE	3898.69, 551.36	11.54, 1.43	
	MEDIAN	4786.8	2.1	
	MIN, MAX	53.6, 18644.1	1.0, 66.3	
	5%, 95%	745.1, 11100.3	1.0, 18.6	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 88 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/L)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	25209.6, 16307.0	27.8, 12.7	
	SD, SE	23299.65, 3295.07	64.53, 8.00	
	MEDIAN	20012.6	7.8	
	MIN, MAX	296.6, 138305.1	5.2, 500.0	
	5%, 95%	2846.6, 63952.2	5.2, 93.7	
	# of BLQ/ALQ Values	0/0	23/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	31105.5, 20863.4	40.2, 14.5	
	SD, SE	25190.66, 3598.67	115.52, 14.33	
	MEDIAN	24988.4	10.4	
	MIN, MAX	279.9, 121371.9	5.2, 881.4	
	5%, 95%	4198.8, 84729.3	5.2, 136.3	
	# of BLQ/ALQ Values	0/0	15/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	26281.4, 18105.1	22.7, 11.4	
	SD, SE	22110.22, 3259.97	47.79, 5.93	
	MEDIAN	21075.5	7.3	
	MIN, MAX	259.6, 121774.7	5.2, 359.5	
	5%, 95%	3659.8, 64930.8	5.2, 81.2	
	# of BLQ/ALQ Values	0/0	25/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	27299.0, 19404.3	30.2, 14.3	
	SD, SE	20284.91, 2868.72	60.02, 7.44	
	MEDIAN	24905.7	10.7	
	MIN, MAX	278.7, 97005.2	5.2, 344.8	
	5%, 95%	3876.6, 57754.9	5.2, 96.8	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	318.3, 240.8		
	SD, SE	225.62, 31.91		
	MEDIAN	247.1		
	MIN, MAX	19.0, 886.1		
	5%, 95%	59.0, 794.9		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	459.8, 323.5		
	SD, SE	434.21, 62.03		
	MEDIAN	361.8		
	MIN, MAX	17.9, 2304.5		
	5%, 95%	100.8, 1254.0		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	403.0, 277.4		
	SD, SE	467.53, 68.93		
	MEDIAN	294.0		
	MIN, MAX	16.6, 2993.5		
	5%, 95%	94.8, 1017.6		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	395.9, 297.1		
	SD, SE	328.26, 46.42		
	MEDIAN	305.0		
	MIN, MAX	17.8, 1912.2		
	5%, 95%	104.8, 924.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	1656.1, 1252.7		
	SD, SE	1173.92, 166.02		
	MEDIAN	1285.7		
	MIN, MAX	98.9, 4610.2		
	5%, 95%	306.7, 4135.8		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	2392.5, 1683.3		
	SD, SE	2259.19, 322.74		
	MEDIAN	1882.5		
	MIN, MAX	93.3, 11990.1		
	5%, 95%	524.4, 6524.6		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	2096.7, 1443.2		
	SD, SE	2432.56, 358.66		
	MEDIAN	1529.8		
	MIN, MAX	86.5, 15575.1		
	5%, 95%	493.0, 5294.6		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	2060.0, 1545.7		
	SD, SE	1707.96, 241.54		
	MEDIAN	1586.8		
	MIN, MAX	92.9, 9949.3		
	5%, 95%	545.2, 4809.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 91 of 264)

Biomarker: Total Cotinine (µg/24hr) Analytical Lab: Harrogate				P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	4878.376, 3421.217	5.320, 2.894	
	SD, SE	3440.7648, 486.5976	8.2060, 1.0178	
	MEDIAN	4470.819	2.265	
	MIN, MAX	44.556, 17099.775	0.570, 46.593	
	5%, 95%	720.720, 10349.625	1.030, 23.940	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	5021.687, 3664.557	6.388, 3.245	
	SD, SE	3238.0901, 462.5843	12.6004, 1.5629	
	MEDIAN	5068.690	2.740	
	MIN, MAX	25.650, 16352.593	0.625, 95.190	
	5%, 95%	735.694, 11710.980	0.915, 17.978	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	5092.021, 3687.215	4.722, 2.969	
	SD, SE	3093.8123, 456.1577	7.0846, 0.8787	
	MEDIAN	5049.495	2.450	
	MIN, MAX	21.379, 13322.126	0.990, 43.940	
	5%, 95%	538.890, 10641.330	1.200, 14.945	
	# of BLQ/ALQ Values	0/0	39/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	4922.139, 3635.756	5.476, 3.257	
	SD, SE	3018.0300, 426.8139	8.0065, 0.9931	
	MEDIAN	5080.985	2.658	
	MIN, MAX	30.528, 13142.481	0.967, 48.539	
	5%, 95%	834.401, 10962.570	1.181, 21.198	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/24hr)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	27684.781, 19415.407	30.188, 16.426	
	SD, SE	19526.3404, 2761.4415	46.5690, 5.7762	
	MEDIAN	25371.898	12.854	
	MIN, MAX	252.855, 97041.223	3.235, 264.415	
	5%, 95%	4090.086, 58734.122	5.845, 135.860	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	28498.074, 20796.363	36.250, 18.415	
	SD, SE	18376.1613, 2625.1659	71.5075, 8.8694	
	MEDIAN	28764.816	15.550	
	MIN, MAX	145.564, 92800.965	3.547, 540.203	
	5%, 95%	4175.063, 66459.812	5.193, 102.025	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	28897.221, 20924.944	26.797, 16.847	
	SD, SE	17557.3848, 2588.6952	40.2052, 4.9868	
	MEDIAN	28655.882	13.904	
	MIN, MAX	121.326, 75603.065	5.618, 249.360	
	5%, 95%	3058.201, 60389.548	6.810, 84.813	
	# of BLQ/ALQ Values	0/0	39/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	27933.141, 20632.919	31.079, 18.485	
	SD, SE	17127.3203, 2422.1689	45.4372, 5.6358	
	MEDIAN	28834.590	15.082	
	MIN, MAX	173.248, 74583.582	5.486, 275.461	
	5%, 95%	4735.227, 62212.586	6.704, 120.299	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((μ g/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	329.496, 262.807		
	SD, SE	255.9854, 36.2018		
	MEDIAN	265.098		
	MIN, MAX	14.852, 1709.978		
	5%, 95%	67.906, 733.236		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	387.177, 295.663		
	SD, SE	348.4011, 49.7716		
	MEDIAN	285.478		
	MIN, MAX	8.550, 1900.378		
	5%, 95%	148.824, 1113.879		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	366.558, 293.920		
	SD, SE	216.7281, 31.9548		
	MEDIAN	305.509		
	MIN, MAX	7.126, 918.949		
	5%, 95%	104.652, 845.604		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	359.150, 292.773		
	SD, SE	239.4210, 33.8592		
	MEDIAN	280.147		
	MIN, MAX	10.176, 1378.107		
	5%, 95%	136.146, 735.186		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	1869.889, 1491.430		
	SD, SE	1452.7166, 205.4451		
	MEDIAN	1504.427		
	MIN, MAX	84.285, 9704.122		
	5%, 95%	385.369, 4161.114		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	2197.228, 1677.887		
	SD, SE	1977.1759, 282.4537		
	MEDIAN	1620.085		
	MIN, MAX	48.521, 10784.643		
	5%, 95%	844.576, 6321.264		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	2080.214, 1667.997		
	SD, SE	1229.9317, 181.3435		
	MEDIAN	1733.765		
	MIN, MAX	40.442, 5215.035		
	5%, 95%	593.900, 4798.800		
	# of BLQ/ALQ Values	0/0		
Overall ^c	N	50		NA
	MEAN, GEO MEAN	2038.178, 1661.487		
	SD, SE	1358.7135, 192.1511		
	MEDIAN	1589.832		
	MIN, MAX	57.749, 7820.754		
	5%, 95%	772.628, 4172.178		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^c Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (µg/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	3.957, 2.835	0.004, NA	
	SD, SE	2.4437, 0.3456	0.0057, 0.0007	
	MEDIAN	3.861	0.002	
	MIN, MAX	0.042, 10.371	0.000, 0.033	
	5%, 95%	0.473, 8.403	0.001, 0.015	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	3.842, 2.829	0.005, NA	
	SD, SE	2.5305, 0.3615	0.0114, 0.0014	
	MEDIAN	3.699	0.002	
	MIN, MAX	0.029, 12.831	0.000, 0.091	
	5%, 95%	0.636, 8.239	0.001, 0.014	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	4.042, 2.957	0.003, 0.002	
	SD, SE	2.6149, 0.3855	0.0044, 0.0005	
	MEDIAN	3.681	0.002	
	MIN, MAX	0.019, 11.859	0.001, 0.025	
	5%, 95%	0.832, 9.415	0.001, 0.008	
	# of BLQ/ALQ Values	0/0	39/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3.950, 2.935	0.004, 0.002	
	SD, SE	2.4396, 0.3450	0.0061, 0.0008	
	MEDIAN	3.804	0.002	
	MIN, MAX	0.030, 10.694	0.001, 0.042	
	5%, 95%	0.733, 8.810	0.001, 0.015	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/mg Creatinine) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	22.456, 16.086	0.021, NA	
	SD, SE	13.8680, 1.9612	0.0321, 0.0040	
	MEDIAN	21.912	0.011	
	MIN, MAX	0.238, 58.855	0.000, 0.187	
	5%, 95%	2.684, 47.687	0.006, 0.085	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	21.801, 16.055	0.028, NA	
	SD, SE	14.3604, 2.0515	0.0647, 0.0080	
	MEDIAN	20.992	0.011	
	MIN, MAX	0.165, 72.816	0.000, 0.516	
	5%, 95%	3.609, 46.756	0.006, 0.079	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	22.940, 16.783	0.019, 0.012	
	SD, SE	14.8394, 2.1880	0.0252, 0.0031	
	MEDIAN	20.887	0.011	
	MIN, MAX	0.108, 67.300	0.006, 0.142	
	5%, 95%	4.722, 53.430	0.006, 0.045	
	# of BLQ/ALQ Values	0/0	39/0	
Overall ^a	N	50	65	<.0001
	MEAN, GEO MEAN	22.417, 16.655	0.023, 0.014	
	SD, SE	13.8448, 1.9579	0.0347, 0.0043	
	MEDIAN	21.585	0.011	
	MIN, MAX	0.170, 60.690	0.004, 0.240	
	5%, 95%	4.162, 49.999	0.006, 0.085	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	0.289, 0.218		
	SD, SE	0.2716, 0.0384		
	MEDIAN	0.205		
	MIN, MAX	0.014, 1.681		
	5%, 95%	0.094, 0.690		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.339, 0.228		
	SD, SE	0.5357, 0.0765		
	MEDIAN	0.198		
	MIN, MAX	0.010, 3.761		
	5%, 95%	0.094, 0.716		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.308, 0.235		
	SD, SE	0.2648, 0.0390		
	MEDIAN	0.232		
	MIN, MAX	0.006, 1.482		
	5%, 95%	0.095, 0.831		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	0.314, 0.237		
	SD, SE	0.3292, 0.0466		
	MEDIAN	0.221		
	MIN, MAX	0.010, 2.177		
	5%, 95%	0.104, 0.584		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 98 of 264)

Biomarker: Total Cotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	1.637, 1.236	
	SD, SE	1.5410, 0.2179	
	MEDIAN	1.164	
	MIN, MAX	0.079, 9.537	
	5%, 95%	0.536, 3.918	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	1.923, 1.295	
	SD, SE	3.0402, 0.4343	
	MEDIAN	1.125	
	MIN, MAX	0.055, 21.344	
	5%, 95%	0.531, 4.063	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	1.746, 1.338	
	SD, SE	1.5031, 0.2216	
	MEDIAN	1.317	
	MIN, MAX	0.036, 8.413	
	5%, 95%	0.542, 4.718	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	1.779, 1.343	
	SD, SE	1.8683, 0.2642	
	MEDIAN	1.255	
	MIN, MAX	0.057, 12.354	
	5%, 95%	0.588, 3.315	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (ng/mL) Analytical Lab: Harrogate				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	3187.2, 2002.0	3.0, 1.8	
	SD, SE	2909.78, 411.50	5.10, 0.63	
	MEDIAN	2020.8	1.0	
	MIN, MAX	31.6, 12610.5	1.0, 35.5	
	5%, 95%	348.7, 10113.6	1.0, 10.7	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	3644.7, 2368.7	3.4, 1.9	
	SD, SE	3403.71, 486.24	5.70, 0.71	
	MEDIAN	2690.9	1.2	
	MIN, MAX	28.5, 18373.7	1.0, 33.4	
	5%, 95%	503.9, 9222.8	1.0, 14.1	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	3056.7, 2160.4	2.5, 1.6	
	SD, SE	2083.46, 307.19	4.43, 0.55	
	MEDIAN	2403.3	1.0	
	MIN, MAX	20.4, 7919.1	1.0, 33.8	
	5%, 95%	390.5, 6761.2	1.0, 6.2	
	# of BLQ/ALQ Values	0/0	39/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3256.3, 2246.5	3.0, 1.9	
	SD, SE	2553.08, 361.06	4.30, 0.53	
	MEDIAN	2699.1	1.2	
	MIN, MAX	26.8, 12581.8	1.0, 27.1	
	5%, 95%	464.3, 7394.7	1.0, 11.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/L) Analytical Lab: Harrogate				P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	18087.2, 11361.6	17.3, 10.1	
	SD, SE	16513.00, 2335.29	28.95, 3.59	
	MEDIAN	11468.1	5.7	
	MIN, MAX	179.3, 71564.6	5.7, 201.5	
	5%, 95%	1978.9, 57394.7	5.7, 60.7	
	# of BLQ/ALQ Values	0/0	33/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	20683.9, 13442.5	19.4, 10.8	
	SD, SE	19316.06, 2759.44	32.33, 4.01	
	MEDIAN	15270.9	6.8	
	MIN, MAX	161.7, 104270.7	5.7, 189.5	
	5%, 95%	2859.6, 52339.4	5.7, 80.0	
	# of BLQ/ALQ Values	0/0	32/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	17347.0, 12260.6	14.3, 9.1	
	SD, SE	11823.64, 1743.30	25.13, 3.12	
	MEDIAN	13638.4	5.7	
	MIN, MAX	115.8, 44940.9	5.7, 191.8	
	5%, 95%	2216.1, 38369.8	5.7, 35.2	
	# of BLQ/ALQ Values	0/0	39/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	18479.7, 12749.4	17.0, 10.7	
	SD, SE	14488.77, 2049.02	24.40, 3.03	
	MEDIAN	15317.2	6.8	
	MIN, MAX	152.3, 71401.7	5.7, 153.6	
	5%, 95%	2634.7, 41965.1	5.7, 64.0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 101 of 264)

Biomarker: Total Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	208.8, 153.8		
	SD, SE	171.02, 24.19		
	MEDIAN	142.9		
	MIN, MAX	10.5, 842.8		
	5%, 95%	56.1, 573.2		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	268.7, 191.1		
	SD, SE	242.85, 34.69		
	MEDIAN	191.9		
	MIN, MAX	9.5, 1226.1		
	5%, 95%	57.9, 918.7		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	244.5, 172.2		
	SD, SE	227.66, 33.57		
	MEDIAN	160.0		
	MIN, MAX	6.8, 1140.3		
	5%, 95%	61.5, 824.2		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	239.5, 179.8		
	SD, SE	188.32, 26.63		
	MEDIAN	180.5		
	MIN, MAX	8.9, 885.7		
	5%, 95%	58.7, 647.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	1184.7, 872.8		
	SD, SE	970.51, 137.25		
	MEDIAN	810.6		
	MIN, MAX	59.8, 4782.9		
	5%, 95%	318.3, 3252.9		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	1524.6, 1084.6		
	SD, SE	1378.13, 196.68		
	MEDIAN	1088.8		
	MIN, MAX	53.9, 6957.9		
	5%, 95%	328.4, 5213.5		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	1387.3, 977.3		
	SD, SE	1291.97, 190.49		
	MEDIAN	907.7		
	MIN, MAX	38.6, 6471.0		
	5%, 95%	349.2, 4677.2		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	1359.4, 1020.2		
	SD, SE	1068.71, 151.14		
	MEDIAN	1024.4		
	MIN, MAX	50.8, 5026.3		
	5%, 95%	333.1, 3674.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (µg/24hr) Analytical Lab: Harrogate				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	2388.232, 1566.128	5.178, 2.339	
	SD, SE	1770.0820, 250.3274	13.2947, 1.6490	
	MEDIAN	2032.229	1.980	
	MIN, MAX	22.137, 6337.875	0.530, 88.160	
	5%, 95%	152.361, 5830.265	0.800, 17.248	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	2506.711, 1693.852	8.023, 2.287	
	SD, SE	1845.8417, 263.6917	42.9602, 5.3286	
	MEDIAN	2099.049	2.025	
	MIN, MAX	10.710, 9552.459	0.625, 348.555	
	5%, 95%	192.780, 5810.675	0.815, 7.128	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	2737.439, 1824.195	2.764, 2.222	
	SD, SE	1983.6441, 292.4724	2.6887, 0.3335	
	MEDIAN	2327.148	2.064	
	MIN, MAX	10.061, 7734.320	0.750, 19.760	
	5%, 95%	288.769, 7314.615	0.990, 7.224	
	# of BLQ/ALQ Values	0/0	51/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	2497.610, 1731.917	5.322, 2.469	
	SD, SE	1659.2686, 234.6560	17.3113, 2.1472	
	MEDIAN	2046.091	2.143	
	MIN, MAX	14.303, 6909.321	0.967, 138.186	
	5%, 95%	172.571, 5294.825	1.057, 11.448	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (nmol/24hr)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	14723.452, 9655.183	31.925, 14.418	
	SD, SE	10912.5555, 1543.2684	81.9620, 10.1661	
	MEDIAN	12528.692	12.207	
	MIN, MAX	136.475, 39072.999	3.267, 543.506	
	5%, 95%	939.306, 35943.584	4.932, 106.334	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	15453.873, 10442.598	49.460, 14.099	
	SD, SE	11379.6144, 1625.6592	264.8496, 32.8505	
	MEDIAN	12940.637	12.484	
	MIN, MAX	66.027, 58890.910	3.853, 2148.842	
	5%, 95%	1188.489, 35822.811	5.024, 43.944	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	16876.314, 11246.162	17.039, 13.700	
	SD, SE	12229.1660, 1803.0921	16.5761, 2.0560	
	MEDIAN	14346.868	12.725	
	MIN, MAX	62.026, 47682.083	4.624, 121.820	
	5%, 95%	1780.261, 45094.601	6.103, 44.536	
	# of BLQ/ALQ Values	0/0	51/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	15397.769, 10677.263	32.808, 15.224	
	SD, SE	10229.3910, 1446.6543	106.7245, 13.2375	
	MEDIAN	12614.151	13.214	
	MIN, MAX	88.176, 42595.964	5.960, 851.919	
	5%, 95%	1063.898, 32642.594	6.514, 70.579	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine ((μ g/24hr)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	NA
	MEAN, GEO MEAN	158.841, 120.305	
	SD, SE	121.2265, 17.1440	
	MEDIAN	141.516	
	MIN, MAX	7.379, 621.350	
	5%, 95%	28.884, 416.448	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	NA
	MEAN, GEO MEAN	205.584, 136.663	
	SD, SE	277.5279, 39.6468	
	MEDIAN	139.937	
	MIN, MAX	3.570, 1882.398	
	5%, 95%	46.464, 569.535	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	NA
	MEAN, GEO MEAN	185.832, 145.413	
	SD, SE	113.3303, 16.7096	
	MEDIAN	170.006	
	MIN, MAX	3.354, 543.137	
	5%, 95%	41.253, 411.403	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	NA
	MEAN, GEO MEAN	180.458, 141.547	
	SD, SE	143.6449, 20.3145	
	MEDIAN	143.212	
	MIN, MAX	4.768, 921.368	
	5%, 95%	53.275, 367.479	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 106 of 264)

Biomarker: Total Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	979.256, 741.681		
	SD, SE	747.3612, 105.6928		
	MEDIAN	872.441		
	MIN, MAX	45.492, 3830.625		
	5%, 95%	178.070, 2567.399		
Week 2	# of BLQ/ALQ Values	0/0		NA
	N	49		
	MEAN, GEO MEAN	1267.426, 842.527		
	SD, SE	1710.9592, 244.4227		
	MEDIAN	862.709		
	MIN, MAX	22.009, 11604.981		
Week 3	5%, 95%	286.451, 3511.183		NA
	# of BLQ/ALQ Values	0/0		
	N	46		
	MEAN, GEO MEAN	1145.652, 896.469		
	SD, SE	698.6815, 103.0150		
	MEDIAN	1048.089		
Overall ^b	MIN, MAX	20.675, 3348.442		NA
	5%, 95%	254.323, 2536.296		
	# of BLQ/ALQ Values	0/0		
	N	50		
	MEAN, GEO MEAN	1112.524, 872.634		
	SD, SE	885.5711, 125.2387		
Overall ^c	MEDIAN	882.901		NA
	MIN, MAX	29.392, 5680.232		
	5%, 95%	328.440, 2265.509		
	# of BLQ/ALQ Values	0/0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (ug/mg Creatinine)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	2.020, 1.298	0.003, NA	
	SD, SE	1.7387, 0.2459	0.0076, 0.0009	
	MEDIAN	1.727	0.002	
	MIN, MAX	0.021, 9.353	0.000, 0.044	
	5%, 95%	0.100, 5.254	0.000, 0.011	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1.974, 1.307	0.007, NA	
	SD, SE	1.6781, 0.2397	0.0411, 0.0051	
	MEDIAN	1.686	0.001	
	MIN, MAX	0.012, 7.495	0.000, 0.333	
	5%, 95%	0.144, 6.431	0.000, 0.004	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	2.100, 1.463	0.002, NA	
	SD, SE	1.3912, 0.2051	0.0016, 0.0002	
	MEDIAN	2.056	0.002	
	MIN, MAX	0.009, 5.794	0.000, 0.011	
	5%, 95%	0.200, 4.966	0.000, 0.004	
	# of BLQ/ALQ Values	0/0	51/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	2.027, 1.398	0.004, NA	
	SD, SE	1.4655, 0.2073	0.0155, 0.0019	
	MEDIAN	1.811	0.002	
	MIN, MAX	0.014, 6.341	0.000, 0.126	
	5%, 95%	0.156, 5.620	0.000, 0.008	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 108 of 264)

Biomarker: Total Nicotine (nmol/mg Creatinine) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	12.456, 8.001	0.021, NA	
	SD, SE	10.7192, 1.5159	0.0466, 0.0058	
	MEDIAN	10.644	0.012	
	MIN, MAX	0.129, 57.661	0.000, 0.271	
	5%, 95%	0.617, 32.391	0.000, 0.068	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	12.170, 8.060	0.044, NA	
	SD, SE	10.3455, 1.4779	0.2535, 0.0314	
	MEDIAN	10.394	0.006	
	MIN, MAX	0.074, 46.207	0.000, 2.053	
	5%, 95%	0.888, 39.647	0.000, 0.025	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	12.945, 9.019	0.012, NA	
	SD, SE	8.5770, 1.2646	0.0100, 0.0012	
	MEDIAN	12.673	0.012	
	MIN, MAX	0.055, 35.720	0.000, 0.068	
	5%, 95%	1.233, 30.615	0.000, 0.025	
	# of BLQ/ALQ Values	0/0	51/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	12.496, 8.617	0.026, 0.011	
	SD, SE	9.0349, 1.2777	0.0960, 0.0119	
	MEDIAN	11.165	0.010	
	MIN, MAX	0.086, 39.094	0.002, 0.779	
	5%, 95%	0.960, 34.649	0.002, 0.049	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 109 of 264)

Biomarker: Total Nicotine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	0.154, 0.100		
	SD, SE	0.2594, 0.0367		
	MEDIAN	0.095		
	MIN, MAX	0.007, 1.871		
	5%, 95%	0.028, 0.288		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	0.202, 0.105		
	SD, SE	0.5228, 0.0747		
	MEDIAN	0.107		
	MIN, MAX	0.004, 3.726		
	5%, 95%	0.033, 0.375		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	0.149, 0.117		
	SD, SE	0.1015, 0.0150		
	MEDIAN	0.125		
	MIN, MAX	0.003, 0.484		
	5%, 95%	0.029, 0.393		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	50		NA
	MEAN, GEO MEAN	0.168, 0.115		
	SD, SE	0.2771, 0.0392		
	MEDIAN	0.110		
	MIN, MAX	0.005, 2.014		
	5%, 95%	0.036, 0.296		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 110 of 264)

Biomarker: Total Nicotine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	NA
	MEAN, GEO MEAN	0.950, 0.615	
	SD, SE	1.5985, 0.2261	
	MEDIAN	0.583	
	MIN, MAX	0.043, 11.532	
	5%, 95%	0.175, 1.776	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	NA
	MEAN, GEO MEAN	1.245, 0.650	
	SD, SE	3.2226, 0.4604	
	MEDIAN	0.662	
	MIN, MAX	0.025, 22.968	
	5%, 95%	0.205, 2.310	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	NA
	MEAN, GEO MEAN	0.921, 0.719	
	SD, SE	0.6259, 0.0923	
	MEDIAN	0.767	
	MIN, MAX	0.018, 2.983	
	5%, 95%	0.176, 2.422	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	NA
	MEAN, GEO MEAN	1.035, 0.705	
	SD, SE	1.7079, 0.2415	
	MEDIAN	0.682	
	MIN, MAX	0.029, 12.412	
	5%, 95%	0.220, 1.824	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 111 of 264)

Biomarker: Total Nicotine (ng/mL) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	1612.6, 916.5	2.4, 1.4	
	SD, SE	1653.11, 233.78	4.50, 0.56	
	MEDIAN	1000.4	1.0	
	MIN, MAX	15.7, 8096.4	1.0, 23.2	
	5%, 95%	88.4, 5070.3	1.0, 8.8	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	1794.7, 1094.9	3.3, 1.3	
	SD, SE	1855.53, 265.08	15.04, 1.87	
	MEDIAN	1304.2	1.0	
	MIN, MAX	11.9, 10733.1	1.0, 122.3	
	5%, 95%	151.2, 5120.6	1.0, 5.1	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	1611.1, 1068.8	1.5, 1.2	
	SD, SE	1234.16, 181.97	1.87, 0.23	
	MEDIAN	1301.9	1.0	
	MIN, MAX	9.6, 4831.6	1.0, 15.2	
	5%, 95%	253.9, 3911.0	1.0, 2.1	
	# of BLQ/ALQ Values	0/0	51/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	1646.9, 1057.4	2.4, 1.4	
	SD, SE	1449.86, 205.04	6.13, 0.76	
	MEDIAN	1216.9	1.0	
	MIN, MAX	12.4, 7887.0	1.0, 48.6	
	5%, 95%	163.9, 3865.6	1.0, 4.5	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 112 of 264)

Biomarker: Total Nicotine (nmol/L) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	9941.7, 5650.1	15.0, 8.9	
	SD, SE	10191.41, 1441.28	27.75, 3.44	
	MEDIAN	6167.2	6.2	
	MIN, MAX	96.8, 49914.3	6.2, 143.0	
	5%, 95%	545.0, 31258.4	6.2, 54.3	
	# of BLQ/ALQ Values	0/0	43/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	11064.6, 6750.1	20.6, 8.3	
	SD, SE	11439.34, 1634.19	92.70, 11.50	
	MEDIAN	8040.4	6.2	
	MIN, MAX	73.4, 66169.6	6.2, 754.0	
	5%, 95%	932.1, 31568.5	6.2, 31.4	
	# of BLQ/ALQ Values	0/0	50/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	9932.6, 6589.5	9.0, 7.4	
	SD, SE	7608.62, 1121.83	11.51, 1.43	
	MEDIAN	8025.9	6.2	
	MIN, MAX	59.2, 29786.8	6.2, 93.7	
	5%, 95%	1565.3, 24111.3	6.2, 12.9	
	# of BLQ/ALQ Values	0/0	51/0	
Overall*	N	50	65	<.0001
	MEAN, GEO MEAN	10152.9, 6518.8	14.8, 8.7	
	SD, SE	8938.40, 1264.08	37.79, 4.69	
	MEDIAN	7502.2	6.2	
	MIN, MAX	76.5, 48623.6	6.2, 299.8	
	5%, 95%	1010.2, 23831.4	6.2, 28.0	

^a P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 113 of 264)

Biomarker: Total Nicotine (ng/mL/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	104.0, 70.4		
	SD, SE	96.79, 13.69		
	MEDIAN	75.1		
	MIN, MAX	5.2, 468.8		
	5%, 95%	19.4, 323.6		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	141.4, 88.3		
	SD, SE	190.40, 27.20		
	MEDIAN	83.4		
	MIN, MAX	4.0, 1214.5		
	5%, 95%	24.4, 403.2		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	119.8, 85.2		
	SD, SE	99.86, 14.72		
	MEDIAN	87.0		
	MIN, MAX	3.2, 464.9		
	5%, 95%	22.4, 322.1		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	119.8, 85.9		
	SD, SE	114.41, 16.18		
	MEDIAN	80.5		
	MIN, MAX	4.1, 667.7		
	5%, 95%	28.7, 325.3		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 114 of 264)

Biomarker: Total Nicotine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	641.2, 434.0		
	SD, SE	596.70, 84.39		
	MEDIAN	463.0		
	MIN, MAX	32.3, 2889.8		
	5%, 95%	119.9, 1995.1		
Week 2	# of BLQ/ALQ Values	0/0		NA
	N	49		
	MEAN, GEO MEAN	871.9, 544.6		
	SD, SE	1173.74, 167.68		
	MEDIAN	514.2		
	MIN, MAX	24.5, 7487.1		
Week 3	5%, 95%	150.5, 2485.9		NA
	# of BLQ/ALQ Values	0/0		
	N	46		
	MEAN, GEO MEAN	738.5, 525.3		
	SD, SE	615.68, 90.78		
	MEDIAN	535.8		
Overall [*]	MIN, MAX	19.7, 2866.2		NA
	5%, 95%	137.9, 1985.8		
	# of BLQ/ALQ Values	0/0		
	N	50		
	MEAN, GEO MEAN	738.5, 529.5		
	SD, SE	705.29, 99.74		
	MEDIAN	496.1		
	MIN, MAX	25.5, 4116.1		
	5%, 95%	176.9, 2005.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 115 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/24hr)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	5745.431, 3951.124	6.964, 3.581	
	SD, SE	4337.8610, 613.4662	11.5984, 1.4386	
	MEDIAN	5379.732	2.800	
	MIN, MAX	42.441, 20367.215	0.855, 67.936	
	5%, 95%	645.000, 15778.245	1.030, 30.820	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	6615.884, 4719.000	9.250, 4.155	
	SD, SE	4263.6442, 609.0920	20.6533, 2.5617	
	MEDIAN	6368.085	2.910	
	MIN, MAX	24.210, 18154.368	0.750, 152.550	
	5%, 95%	722.866, 15032.830	1.023, 31.960	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	6170.891, 4344.157	6.512, 3.646	
	SD, SE	4218.9830, 622.0551	11.2227, 1.3920	
	MEDIAN	5068.953	2.890	
	MIN, MAX	21.379, 15121.480	0.990, 72.800	
	5%, 95%	976.686, 14222.565	1.300, 31.610	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	6093.854, 4444.837	7.576, 4.132	
	SD, SE	3968.4962, 561.2301	12.7435, 1.5806	
	MEDIAN	5310.133	3.182	
	MIN, MAX	29.343, 17222.174	1.038, 76.940	
	5%, 95%	696.229, 12433.240	1.303, 33.167	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 116 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/24hr) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	29893.480, 20557.701	36.235, 18.631	
	SD, SE	22569.8906, 3191.8645	60.3466, 7.4851	
	MEDIAN	27990.743	14.568	
	MIN, MAX	220.821, 105970.620	4.449, 353.471	
	5%, 95%	3355.935, 82094.209	5.359, 160.356	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	34422.443, 24552.957	48.129, 21.619	
	SD, SE	22183.7406, 3169.1058	107.4591, 13.3287	
	MEDIAN	33133.146	15.141	
	MIN, MAX	125.965, 94457.177	3.902, 793.718	
	5%, 95%	3761.072, 78215.814	5.323, 166.288	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	32107.148, 22602.652	33.883, 18.972	
	SD, SE	21951.3688, 3236.5528	58.3918, 7.2426	
	MEDIAN	26373.760	15.037	
	MIN, MAX	111.235, 78677.060	5.151, 378.778	
	5%, 95%	5081.697, 74000.006	6.764, 164.467	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	31706.321, 23126.495	39.416, 21.501	
	SD, SE	20648.0857, 2920.0803	66.3047, 8.2241	
	MEDIAN	27628.619	16.556	
	MIN, MAX	152.674, 89606.973	5.402, 400.319	
	5%, 95%	3622.478, 64690.148	6.778, 172.570	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (($\mu\text{g}/24\text{hr}$)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	385.100, 303.513		
	SD, SE	266.5916, 37.7017		
	MEDIAN	325.512		
	MIN, MAX	14.147, 1577.825		
	5%, 95%	71.775, 899.285		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	506.178, 380.737		
	SD, SE	418.8634, 59.8376		
	MEDIAN	400.405		
	MIN, MAX	8.070, 2529.445		
	5%, 95%	164.300, 1157.695		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	436.853, 346.287		
	SD, SE	270.9947, 39.9560		
	MEDIAN	371.128		
	MIN, MAX	7.126, 1230.107		
	5%, 95%	159.486, 1036.347		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	442.816, 355.555		
	SD, SE	277.0733, 39.1841		
	MEDIAN	377.916		
	MIN, MAX	9.781, 1385.359		
	5%, 95%	148.070, 1006.597		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 118 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	2003.674, 1579.178		
	SD, SE	1387.0757, 196.1621		
	MEDIAN	1693.636		
	MIN, MAX	73.607, 8209.421		
	5%, 95%	373.446, 4678.980		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	2633.642, 1980.976		
	SD, SE	2179.3464, 311.3352		
	MEDIAN	2083.307		
	MIN, MAX	41.988, 13160.703		
	5%, 95%	854.853, 6023.487		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	2272.944, 1801.733		
	SD, SE	1409.9852, 207.8910		
	MEDIAN	1930.976		
	MIN, MAX	37.078, 6400.244		
	5%, 95%	829.805, 5392.114		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	2303.971, 1849.953		
	SD, SE	1441.6122, 203.8748		
	MEDIAN	1966.297		
	MIN, MAX	50.891, 7208.023		
	5%, 95%	770.409, 5237.322		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	4.766, 3.274	0.005, NA	
	SD, SE	3.4639, 0.4899	0.0080, 0.0010	
	MEDIAN	4.258	0.002	
	MIN, MAX	0.040, 14.351	0.000, 0.042	
	5%, 95%	0.300, 12.478	0.001, 0.019	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	5.168, 3.642	0.006, NA	
	SD, SE	3.6621, 0.5232	0.0123, 0.0015	
	MEDIAN	4.126	0.002	
	MIN, MAX	0.027, 15.297	0.000, 0.079	
	5%, 95%	0.400, 12.899	0.001, 0.019	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	5.034, 3.484	0.004, 0.003	
	SD, SE	3.6689, 0.5410	0.0062, 0.0008	
	MEDIAN	3.689	0.002	
	MIN, MAX	0.019, 15.542	0.001, 0.041	
	5%, 95%	0.770, 11.642	0.001, 0.017	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	4.971, 3.566	0.005, 0.003	
	SD, SE	3.4521, 0.4882	0.0075, 0.0009	
	MEDIAN	4.113	0.002	
	MIN, MAX	0.029, 14.264	0.001, 0.037	
	5%, 95%	0.497, 12.705	0.001, 0.019	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	24.797, 17.032	0.026, NA	
	SD, SE	18.0226, 2.5488	0.0418, 0.0052	
	MEDIAN	22.155	0.010	
	MIN, MAX	0.208, 74.668	0.000, 0.219	
	5%, 95%	1.561, 64.923	0.005, 0.099	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	26.891, 18.948	0.032, NA	
	SD, SE	19.0536, 2.7219	0.0640, 0.0079	
	MEDIAN	21.468	0.010	
	MIN, MAX	0.140, 79.590	0.000, 0.411	
	5%, 95%	2.081, 67.113	0.005, 0.099	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	26.191, 18.128	0.022, 0.013	
	SD, SE	19.0893, 2.8146	0.0325, 0.0040	
	MEDIAN	19.194	0.010	
	MIN, MAX	0.099, 80.865	0.005, 0.213	
	5%, 95%	4.006, 60.573	0.005, 0.088	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	25.862, 18.548	0.027, 0.015	
	SD, SE	17.9615, 2.5401	0.0389, 0.0048	
	MEDIAN	21.398	0.012	
	MIN, MAX	0.149, 74.215	0.003, 0.194	
	5%, 95%	2.586, 66.106	0.005, 0.099	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	NA
	MEAN, GEO MEAN	0.340, 0.251	
	SD, SE	0.3073, 0.0435	
	MEDIAN	0.266	
	MIN, MAX	0.013, 1.777	
	5%, 95%	0.060, 0.957	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	NA
	MEAN, GEO MEAN	0.450, 0.294	
	SD, SE	0.7038, 0.1005	
	MEDIAN	0.286	
	MIN, MAX	0.009, 5.006	
	5%, 95%	0.094, 0.914	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	NA
	MEAN, GEO MEAN	0.376, 0.277	
	SD, SE	0.3241, 0.0478	
	MEDIAN	0.279	
	MIN, MAX	0.006, 1.768	
	5%, 95%	0.107, 0.928	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	NA
	MEAN, GEO MEAN	0.391, 0.285	
	SD, SE	0.4161, 0.0588	
	MEDIAN	0.312	
	MIN, MAX	0.009, 2.850	
	5%, 95%	0.116, 1.063	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine)/cigarette per day		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	1.771, 1.308	
	SD, SE	1.5987, 0.2261	
	MEDIAN	1.384	
	MIN, MAX	0.069, 9.247	
	5%, 95%	0.310, 4.979	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	2.342, 1.529	
	SD, SE	3.6619, 0.5231	
	MEDIAN	1.485	
	MIN, MAX	0.047, 26.046	
	5%, 95%	0.487, 4.754	
	# of BLQ/ALQ Values	0/0	
Week 3	N	46	
	MEAN, GEO MEAN	1.955, 1.445	
	SD, SE	1.6865, 0.2487	
	MEDIAN	1.452	
	MIN, MAX	0.033, 9.197	
	5%, 95%	0.558, 4.830	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	2.034, 1.486	
	SD, SE	2.1649, 0.3062	
	MEDIAN	1.622	
	MIN, MAX	0.050, 14.830	
	5%, 95%	0.603, 5.530	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 123 of 264)

Biomarker: Trans-3-hydroxycotinine (ng/mL)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	3549.7, 2312.1	4.4, 2.2	
	SD, SE	3173.27, 448.77	9.97, 1.24	
	MEDIAN	3110.5	1.4	
	MIN, MAX	30.1, 17333.8	1.0, 77.2	
	5%, 95%	422.2, 9882.6	1.0, 16.4	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	4688.4, 3050.3	6.2, 2.4	
	SD, SE	3986.05, 569.44	17.70, 2.19	
	MEDIAN	3435.7	1.7	
	MIN, MAX	26.9, 18865.3	1.0, 135.0	
	5%, 95%	692.4, 13308.1	1.0, 21.4	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	3636.9, 2545.4	3.6, 2.0	
	SD, SE	2820.50, 415.86	7.31, 0.91	
	MEDIAN	3045.4	1.3	
	MIN, MAX	20.4, 15599.2	1.0, 56.0	
	5%, 95%	525.1, 8394.0	1.0, 10.9	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3928.4, 2775.7	4.7, 2.4	
	SD, SE	2928.37, 414.13	9.29, 1.15	
	MEDIAN	3463.0	1.8	
	MIN, MAX	25.8, 13970.9	1.0, 52.6	
	5%, 95%	601.4, 8965.5	1.0, 14.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (nmol/L)		Analytical Lab: Harrogate		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	18469.2, 12030.0	23.1, 11.4	
	SD, SE	16510.52, 2334.94	51.89, 6.44	
	MEDIAN	16183.9	7.3	
	MIN, MAX	156.6, 90187.8	5.2, 401.7	
	5%, 95%	2196.7, 51419.2	5.2, 85.3	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	24393.8, 15870.9	32.3, 12.6	
	SD, SE	20739.45, 2962.78	92.07, 11.42	
	MEDIAN	17875.9	8.8	
	MIN, MAX	140.0, 98156.2	5.2, 702.4	
	5%, 95%	3602.6, 69242.0	5.2, 111.3	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	18922.7, 13243.4	18.5, 10.2	
	SD, SE	14675.07, 2163.72	38.06, 4.72	
	MEDIAN	15845.0	6.8	
	MIN, MAX	106.1, 81162.6	5.2, 291.4	
	5%, 95%	2732.1, 43674.0	5.2, 56.7	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	20439.3, 14441.8	24.7, 12.6	
	SD, SE	15236.32, 2154.74	48.35, 6.00	
	MEDIAN	18017.8	9.3	
	MIN, MAX	134.2, 72690.6	5.2, 273.7	
	5%, 95%	3129.3, 46647.3	5.2, 74.6	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	237.0, 177.6		
	SD, SE	172.16, 24.35		
	MEDIAN	195.5		
	MIN, MAX	10.0, 648.2		
	5%, 95%	47.8, 607.6		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	356.4, 246.1		
	SD, SE	330.14, 47.16		
	MEDIAN	271.8		
	MIN, MAX	9.0, 1631.9		
	5%, 95%	82.2, 942.6		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	291.2, 202.9		
	SD, SE	303.79, 44.79		
	MEDIAN	197.5		
	MIN, MAX	6.8, 1850.6		
	5%, 95%	65.3, 820.7		
	# of BLQ/ALQ Values	0/0		
Overall*	N	50		NA
	MEAN, GEO MEAN	297.1, 220.8		
	SD, SE	239.90, 33.93		
	MEDIAN	224.3		
	MIN, MAX	8.6, 1263.3		
	5%, 95%	78.0, 801.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	50	
	MEAN, GEO MEAN	1232.9, 924.1	
	SD, SE	895.77, 126.68	
	MEDIAN	1017.1	
	MIN, MAX	52.2, 3372.8	
	5%, 95%	248.6, 3161.5	
Week 2	# of BLQ/ALQ Values	0/0	
	N	49	
	MEAN, GEO MEAN	1854.4, 1280.5	
	SD, SE	1717.72, 245.39	
	MEDIAN	1414.4	
	MIN, MAX	46.7, 8490.8	
Week 3	5%, 95%	427.4, 4904.3	
	# of BLQ/ALQ Values	0/0	
	N	46	
	MEAN, GEO MEAN	1515.2, 1055.7	
	SD, SE	1580.61, 233.05	
	MEDIAN	1027.4	
Overall*	MIN, MAX	35.4, 9628.8	
	5%, 95%	339.8, 4269.9	
	# of BLQ/ALQ Values	0/0	
	N	50	
	MEAN, GEO MEAN	1545.7, 1148.6	
	SD, SE	1248.24, 176.53	
Overall*	MEDIAN	1167.1	
	MIN, MAX	44.8, 6573.1	
	5%, 95%	405.8, 4168.4	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/24hr)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	53	<.0001
	MEAN, GEO MEAN	11096.179, 6918.753	9.268, NA	
	SD, SE	10472.8752, 1496.1250	17.2617, 2.3711	
	MEDIAN	8366.015	2.106	
	MIN, MAX	197.400, 56537.828	0.000, 86.504	
	5%, 95%	757.770, 26230.442	0.000, 52.260	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	59	<.0001
	MEAN, GEO MEAN	10165.213, 7180.455	13.668, NA	
	SD, SE	7498.0883, 1071.1555	30.4127, 3.9594	
	MEDIAN	8992.596	1.575	
	MIN, MAX	126.000, 38811.750	0.000, 202.270	
	5%, 95%	622.537, 24231.808	0.000, 62.122	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	45	61	<.0001
	MEAN, GEO MEAN	12310.192, 8164.712	8.349, NA	
	SD, SE	11374.8476, 1695.6622	18.7129, 2.3959	
	MEDIAN	8468.655	1.050	
	MIN, MAX	160.868, 64170.700	0.000, 88.660	
	5%, 95%	1725.522, 31402.440	0.000, 42.273	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	64	<.0001
	MEAN, GEO MEAN	10913.713, 7675.781	10.045, NA	
	SD, SE	8872.2538, 1254.7262	19.3895, 2.4237	
	MEDIAN	9018.318	2.457	
	MIN, MAX	161.423, 49042.882	0.000, 104.787	
	5%, 95%	828.268, 27010.976	0.000, 49.847	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 128 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49		NA
	MEAN, GEO MEAN	695.999, 530.594		
	SD, SE	448.5707, 64.0815		
	MEDIAN	671.090		
	MIN, MAX	43.617, 1884.594		
	5%, 95%	65.800, 1670.809		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	793.931, 579.332		
	SD, SE	811.6069, 115.9438		
	MEDIAN	626.919		
	MIN, MAX	34.585, 5423.915		
	5%, 95%	175.088, 1661.556		
	# of BLQ/ALQ Values	0/0		
Week 3	N	45		NA
	MEAN, GEO MEAN	828.559, 637.667		
	SD, SE	590.4088, 88.0129		
	MEDIAN	673.095		
	MIN, MAX	35.637, 3329.928		
	5%, 95%	236.928, 1723.842		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	769.302, 619.089		
	SD, SE	518.4089, 73.3141		
	MEDIAN	707.376		
	MIN, MAX	37.946, 3355.093		
	5%, 95%	230.597, 1545.608		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	49	53	<.0001
	MEAN, GEO MEAN	8.953, 5.755	0.006, NA	
	SD, SE	7.6799, 1.0971	0.0114, 0.0016	
	MEDIAN	6.754	0.002	
	MIN, MAX	0.182, 37.904	0.000, 0.053	
	5%, 95%	0.365, 24.215	0.000, 0.034	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	59	<.0001
	MEAN, GEO MEAN	8.344, 5.542	0.009, NA	
	SD, SE	7.7423, 1.1060	0.0188, 0.0024	
	MEDIAN	5.726	0.001	
	MIN, MAX	0.141, 37.773	0.000, 0.105	
	5%, 95%	0.539, 24.592	0.000, 0.053	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	45	61	<.0001
	MEAN, GEO MEAN	10.066, 6.491	0.005, NA	
	SD, SE	9.7261, 1.4499	0.0101, 0.0013	
	MEDIAN	6.677	0.001	
	MIN, MAX	0.141, 41.198	0.000, 0.050	
	5%, 95%	1.718, 30.778	0.000, 0.030	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	64	<.0001
	MEAN, GEO MEAN	9.000, 6.118	0.006, NA	
	SD, SE	7.9341, 1.1220	0.0116, 0.0014	
	MEDIAN	6.640	0.002	
	MIN, MAX	0.156, 38.958	0.000, 0.052	
	5%, 95%	0.813, 26.074	0.000, 0.036	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 130 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)/cigarette per day		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	49	
	MEAN, GEO MEAN	0.618, 0.441	
	SD, SE	0.6338, 0.0905	
	MEDIAN	0.507	
	MIN, MAX	0.020, 3.948	
	5%, 95%	0.091, 1.523	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	0.755, 0.447	
	SD, SE	1.5032, 0.2147	
	MEDIAN	0.437	
	MIN, MAX	0.018, 10.734	
	5%, 95%	0.135, 1.381	
	# of BLQ/ALQ Values	0/0	
Week 3	N	45	
	MEAN, GEO MEAN	0.722, 0.507	
	SD, SE	0.8347, 0.1244	
	MEDIAN	0.560	
	MIN, MAX	0.020, 5.679	
	5%, 95%	0.217, 1.231	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	0.700, 0.494	
	SD, SE	0.9391, 0.1328	
	MEDIAN	0.514	
	MIN, MAX	0.019, 6.787	
	5%, 95%	0.177, 1.316	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 131 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/L) Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	49	53	<.0001
	MEAN, GEO MEAN	6895.8, 4024.9	6.0, NA	
	SD, SE	7654.61, 1093.52	14.26, 1.96	
	MEDIAN	5136.9	2.1	
	MIN, MAX	79.6, 48117.3	0.0, 98.3	
	5%, 95%	649.9, 16292.2	0.0, 21.9	
	# of BLQ/ALQ Values	0/0	22/0	
Week 2	N	49	59	<.0001
	MEAN, GEO MEAN	6711.8, 4641.4	8.8, NA	
	SD, SE	5108.69, 729.81	25.07, 3.26	
	MEDIAN	5545.9	1.6	
	MIN, MAX	140.0, 23215.8	0.0, 179.0	
	5%, 95%	596.3, 15749.0	0.0, 38.0	
	# of BLQ/ALQ Values	0/0	17/0	
Week 3	N	45	61	<.0001
	MEAN, GEO MEAN	7528.7, 4762.9	4.5, NA	
	SD, SE	8062.18, 1201.84	10.35, 1.33	
	MEDIAN	5225.9	0.5	
	MIN, MAX	153.5, 40612.0	0.0, 68.2	
	5%, 95%	927.7, 29168.5	0.0, 24.5	
	# of BLQ/ALQ Values	0/0	30/0	
Overall ^b	N	50	64	<.0001
	MEAN, GEO MEAN	6902.1, 4770.7	6.4, NA	
	SD, SE	5566.90, 787.28	14.10, 1.76	
	MEDIAN	5704.9	1.7	
	MIN, MAX	144.5, 25999.9	0.0, 83.3	
	5%, 95%	640.7, 19989.6	0.0, 22.2	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 132 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	49	
	MEAN, GEO MEAN	433.3, 308.7	
	SD, SE	348.28, 49.75	
	MEDIAN	366.9	
	MIN, MAX	39.8, 1603.9	
	5%, 95%	58.1, 1099.4	
	# of BLQ/ALQ Values	0/0	
Week 2	N	49	
	MEAN, GEO MEAN	538.1, 374.5	
	SD, SE	578.57, 82.65	
	MEDIAN	388.1	
	MIN, MAX	33.1, 3499.3	
	5%, 95%	76.7, 1620.3	
	# of BLQ/ALQ Values	0/0	
Week 3	N	45	
	MEAN, GEO MEAN	595.7, 372.0	
	SD, SE	899.83, 134.14	
	MEDIAN	367.3	
	MIN, MAX	15.5, 5946.3	
	5%, 95%	125.4, 1673.6	
	# of BLQ/ALQ Values	0/0	
Overall*	N	50	
	MEAN, GEO MEAN	520.2, 382.8	
	SD, SE	502.97, 71.13	
	MEDIAN	397.4	
	MIN, MAX	35.6, 3376.2	
	5%, 95%	133.6, 1077.6	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439004

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (nmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	7	0.0034
	MEAN, GEO MEAN	8116.241, 7377.365	9.819, 7.923	
	SD, SE	3337.3914, 1362.4844	8.2449, 3.1163	
	MEDIAN	9239.023	7.062	
	MIN, MAX	3100.528, 11659.550	3.720, 27.797	
	5%, 95%	3100.528, 11659.550	3.720, 27.797	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0024
	MEAN, GEO MEAN	8657.223, 8169.359	7.179, 6.747	
	SD, SE	3203.9834, 1308.0207	2.4766, 0.8756	
	MEDIAN	8162.925	7.673	
	MIN, MAX	4574.775, 13936.670	3.224, 10.540	
	5%, 95%	4574.775, 13936.670	3.224, 10.540	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	7331.938, 6175.173	6.454, 6.143	
	SD, SE	4110.3879, 1838.2214	2.2246, 0.8408	
	MEDIAN	7564.865	5.828	
	MIN, MAX	2098.704, 12059.465	3.906, 9.920	
	5%, 95%	2098.704, 12059.465	3.906, 9.920	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	8075.004, 7437.279	7.852, 7.377	
	SD, SE	3105.3617, 1267.7586	2.8719, 1.0154	
	MEDIAN	9221.998	7.854	
	MIN, MAX	3258.002, 10736.417	3.617, 13.134	
	5%, 95%	3258.002, 10736.417	3.617, 13.134	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 134 of 264)

Biomarker: Cotinine (µg/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	7	0.0034
	MEAN, GEO MEAN	1430.082, 1299.892	1.730, 1.396	
	SD, SE	588.0485, 240.0698	1.4529, 0.5492	
	MEDIAN	1627.916	1.244	
	MIN, MAX	546.313, 2054.413	0.655, 4.898	
	5%, 95%	546.313, 2054.413	0.655, 4.898	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0024
	MEAN, GEO MEAN	1525.403, 1439.441	1.265, 1.189	
	SD, SE	564.5419, 230.4733	0.4362, 0.1542	
	MEDIAN	1438.308	1.352	
	MIN, MAX	806.075, 2455.641	0.568, 1.857	
	5%, 95%	806.075, 2455.641	0.568, 1.857	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	1291.888, 1088.066	1.137, 1.082	
	SD, SE	724.2504, 323.8946	0.3920, 0.1482	
	MEDIAN	1332.929	1.027	
	MIN, MAX	369.792, 2124.878	0.688, 1.748	
	5%, 95%	369.792, 2124.878	0.688, 1.748	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	1422.816, 1310.449	1.383, 1.300	
	SD, SE	547.1647, 223.3791	0.5060, 0.1789	
	MEDIAN	1624.916	1.384	
	MIN, MAX	574.060, 1891.757	0.637, 2.314	
	5%, 95%	574.060, 1891.757	0.637, 2.314	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 135 of 264)

Biomarker: Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	480.942, 449.009		
	SD, SE	209.8036, 85.6520		
	MEDIAN	433.268		
	MIN, MAX	278.469, 870.573		
	5%, 95%	278.469, 870.573		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	728.933, 619.083		
	SD, SE	504.0549, 205.7796		
	MEDIAN	577.156		
	MIN, MAX	350.203, 1683.665		
	5%, 95%	350.203, 1683.665		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	744.731, 565.317		
	SD, SE	631.7633, 282.5332		
	MEDIAN	378.243		
	MIN, MAX	249.386, 1741.285		
	5%, 95%	249.386, 1741.285		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	630.928, 552.357		
	SD, SE	372.9587, 152.2598		
	MEDIAN	480.530		
	MIN, MAX	292.686, 1259.423		
	5%, 95%	292.686, 1259.423		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 136 of 264)

Biomarker: Cotinine ((ug/24hr)/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	84.742, 79.115	
	SD, SE	36.9674, 15.0919	
	MEDIAN	76.342	
	MIN, MAX	49.066, 153.395	
	5%, 95%	49.066, 153.395	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	128.438, 109.083	
	SD, SE	88.8144, 36.2583	
	MEDIAN	101.695	
	MIN, MAX	61.706, 296.662	
	5%, 95%	61.706, 296.662	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	131.222, 99.609	
	SD, SE	111.3169, 49.7824	
	MEDIAN	66.646	
	MIN, MAX	43.942, 306.815	
	5%, 95%	43.942, 306.815	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	111.170, 97.325	
	SD, SE	65.7157, 26.8283	
	MEDIAN	84.669	
	MIN, MAX	51.571, 221.911	
	5%, 95%	51.571, 221.911	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	7	0.0032
	MEAN, GEO MEAN	6.206, 5.345	0.006, 0.006	
	SD, SE	3.4820, 1.4215	0.0034, 0.0013	
	MEDIAN	6.151	0.005	
	MIN, MAX	2.553, 11.433	0.003, 0.012	
	5%, 95%	2.553, 11.433	0.003, 0.012	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0024
	MEAN, GEO MEAN	7.082, 6.437	0.005, 0.005	
	SD, SE	3.7617, 1.5357	0.0028, 0.0010	
	MEDIAN	5.586	0.005	
	MIN, MAX	4.231, 14.182	0.002, 0.011	
	5%, 95%	4.231, 14.182	0.002, 0.011	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0049
	MEAN, GEO MEAN	6.752, 6.033	0.005, 0.005	
	SD, SE	3.2634, 1.4594	0.0014, 0.0005	
	MEDIAN	7.282	0.006	
	MIN, MAX	3.016, 9.978	0.003, 0.007	
	5%, 95%	3.016, 9.978	0.003, 0.007	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	6	8	0.0024
	MEAN, GEO MEAN	6.575, 5.962	0.006, 0.006	
	SD, SE	3.0766, 1.2560	0.0018, 0.0006	
	MEDIAN	6.547	0.005	
	MIN, MAX	3.296, 10.966	0.004, 0.009	
	5%, 95%	3.296, 10.966	0.004, 0.009	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (µg/mg Creatinine)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	7	0.0026
	MEAN, GEO MEAN	1.093, 0.942	0.001, 0.001	
	SD, SE	0.6133, 0.2504	0.0005, 0.0002	
	MEDIAN	1.084	0.001	
	MIN, MAX	0.450, 2.014	0.001, 0.002	
	5%, 95%	0.450, 2.014	0.001, 0.002	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0016
	MEAN, GEO MEAN	1.248, 1.134	0.001, NA	
	SD, SE	0.6628, 0.2706	0.0005, 0.0002	
	MEDIAN	0.984	0.001	
	MIN, MAX	0.746, 2.499	0.000, 0.002	
	5%, 95%	0.746, 2.499	0.000, 0.002	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	1.190, 1.063	0.001, 0.001	
	SD, SE	0.5751, 0.2572	0.0000, 0.0000	
	MEDIAN	1.283	0.001	
	MIN, MAX	0.531, 1.758	0.001, 0.001	
	5%, 95%	0.531, 1.758	0.001, 0.001	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	6	8	0.0016
	MEAN, GEO MEAN	1.159, 1.051	0.001, 0.001	
	SD, SE	0.5419, 0.2212	0.0004, 0.0001	
	MEDIAN	1.154	0.001	
	MIN, MAX	0.581, 1.932	0.001, 0.002	
	5%, 95%	0.581, 1.932	0.001, 0.002	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 139 of 264)

Biomarker: Cotinine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6		NA
	MEAN, GEO MEAN	0.371, 0.326		
	SD, SE	0.1949, 0.0796		
	MEDIAN	0.339		
	MIN, MAX	0.147, 0.612		
	5%, 95%	0.147, 0.612		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.574, 0.488		
	SD, SE	0.3286, 0.1342		
	MEDIAN	0.594		
	MIN, MAX	0.212, 1.066		
	5%, 95%	0.212, 1.066		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.726, 0.553		
	SD, SE	0.5784, 0.2587		
	MEDIAN	0.624		
	MIN, MAX	0.168, 1.663		
	5%, 95%	0.168, 1.663		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	0.529, 0.447		
	SD, SE	0.3063, 0.1250		
	MEDIAN	0.529		
	MIN, MAX	0.176, 0.994		
	5%, 95%	0.176, 0.994		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 140 of 264)

Biomarker: Cotinine ((ug/mg Creatinine)/cigarette per day)		Analytical Lab: INBiFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.065, 0.057		
	SD, SE	0.0345, 0.0141		
	MEDIAN	0.060		
	MIN, MAX	0.026, 0.108		
	5%, 95%	0.026, 0.108		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.101, 0.086		
	SD, SE	0.0581, 0.0237		
	MEDIAN	0.105		
	MIN, MAX	0.037, 0.188		
	5%, 95%	0.037, 0.188		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.128, 0.098		
	SD, SE	0.1018, 0.0455		
	MEDIAN	0.110		
	MIN, MAX	0.030, 0.293		
	5%, 95%	0.030, 0.293		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	0.093, 0.079		
	SD, SE	0.0540, 0.0220		
	MEDIAN	0.094		
	MIN, MAX	0.031, 0.175		
	5%, 95%	0.031, 0.175		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 141 of 264)

Biomarker: Cotinine (nmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	7	0.0021
	MEAN, GEO MEAN	5138.7, 4383.0	5.6, 4.1	
	SD, SE	3563.54, 1454.81	6.73, 2.54	
	MEDIAN	4048.8	3.1	
	MIN, MAX	2279.8, 12007.9	3.1, 20.9	
	5%, 95%	2279.8, 12007.9	3.1, 20.9	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0008
	MEAN, GEO MEAN	5341.9, 4848.5	3.1, 3.1	
	SD, SE	2622.04, 1070.44	0.00, 0.00	
	MEDIAN	4597.2	3.1	
	MIN, MAX	2527.5, 9702.2	3.1, 3.1	
	5%, 95%	2527.5, 9702.2	3.1, 3.1	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	4021.5, 3476.2	3.1, 3.1	
	SD, SE	2413.87, 1079.52	0.00, 0.00	
	MEDIAN	3087.7	3.1	
	MIN, MAX	1520.8, 7780.3	3.1, 3.1	
	5%, 95%	1520.8, 7780.3	3.1, 3.1	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0012
	MEAN, GEO MEAN	4959.3, 4381.0	3.8, 3.5	
	SD, SE	2782.63, 1136.00	2.09, 0.74	
	MEDIAN	4206.5	3.1	
	MIN, MAX	2109.4, 9830.1	3.1, 9.0	
	5%, 95%	2109.4, 9830.1	3.1, 9.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 142 of 264)

Biomarker: Cotinine (ng/mL)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	7	0.0021
	MEAN, GEO MEAN	905.4, 772.3	1.0, 0.7	
	SD, SE	627.91, 256.34	1.21, 0.46	
	MEDIAN	713.4	0.5	
	MIN, MAX	401.7, 2115.8	0.5, 3.7	
	5%, 95%	401.7, 2115.8	0.5, 3.7	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	8	0.0008
	MEAN, GEO MEAN	941.2, 854.3	0.5, 0.5	
	SD, SE	462.01, 188.61	0.00, 0.00	
	MEDIAN	810.0	0.5	
	MIN, MAX	445.3, 1709.5	0.5, 0.5	
	5%, 95%	445.3, 1709.5	0.5, 0.5	
	# of BLQ/ALQ Values	0/0	8/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	708.6, 612.5	0.5, 0.5	
	SD, SE	425.31, 190.20	0.00, 0.00	
	MEDIAN	544.1	0.5	
	MIN, MAX	268.0, 1370.9	0.5, 0.5	
	5%, 95%	268.0, 1370.9	0.5, 0.5	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0012
	MEAN, GEO MEAN	873.9, 771.9	0.6, 0.6	
	SD, SE	490.31, 200.17	0.39, 0.14	
	MEDIAN	741.2	0.5	
	MIN, MAX	371.7, 1732.1	0.5, 1.6	
	5%, 95%	371.7, 1732.1	0.5, 1.6	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 143 of 264)

Biomarker: Cotinine ((nmol/L)/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	349.2, 266.8	
	SD, SE	330.69, 135.00	
	MEDIAN	202.2	
	MIN, MAX	144.2, 1000.7	
	5%, 95%	144.2, 1000.7	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	445.7, 367.5	
	SD, SE	306.85, 125.27	
	MEDIAN	303.7	
	MIN, MAX	176.9, 882.0	
	5%, 95%	176.9, 882.0	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	405.0, 318.2	
	SD, SE	303.96, 135.93	
	MEDIAN	253.5	
	MIN, MAX	154.4, 809.9	
	5%, 95%	154.4, 809.9	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	393.9, 330.4	
	SD, SE	265.41, 108.35	
	MEDIAN	295.7	
	MIN, MAX	167.2, 843.7	
	5%, 95%	167.2, 843.7	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 144 of 264)

Biomarker: Cotinine (ng/mL)/cigarette per day		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	61.5, 47.0		
	SD, SE	58.26, 23.78		
	MEDIAN	35.7		
	MIN, MAX	25.4, 176.3		
	5%, 95%	25.4, 176.3		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	78.5, 64.7		
	SD, SE	54.07, 22.07		
	MEDIAN	53.5		
	MIN, MAX	31.2, 155.4		
	5%, 95%	31.2, 155.4		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	71.4, 56.1		
	SD, SE	53.54, 23.94		
	MEDIAN	44.7		
	MIN, MAX	27.2, 142.7		
	5%, 95%	27.2, 142.7		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	69.4, 58.2		
	SD, SE	46.72, 19.07		
	MEDIAN	52.2		
	MIN, MAX	29.5, 148.6		
	5%, 95%	29.5, 148.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 145 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	5	0.0081
	MEAN, GEO MEAN	13422.559, 9233.175	17.266, 16.074	
	SD, SE	8208.4761, 3351.0963	7.0648, 3.1595	
	MEDIAN	12610.540	16.116	
	MIN, MAX	797.096, 24184.869	9.480, 25.343	
	5%, 95%	797.096, 24184.869	9.480, 25.343	
	# of BLQ/ALQ Values	0/0	5/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	13285.550, 10994.917	18.424, 17.167	
	SD, SE	6499.2379, 2653.3027	6.8053, 2.5722	
	MEDIAN	14471.774	21.725	
	MIN, MAX	2320.420, 19683.264	8.216, 26.860	
	5%, 95%	2320.420, 19683.264	8.216, 26.860	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	6	0.0081
	MEAN, GEO MEAN	11027.932, 6237.609	14.976, 14.454	
	SD, SE	7390.1613, 3304.9806	4.5130, 1.8424	
	MEDIAN	12845.595	14.536	
	MIN, MAX	339.066, 19365.855	9.954, 22.910	
	5%, 95%	339.066, 19365.855	9.954, 22.910	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	12803.241, 9518.732	17.115, 16.315	
	SD, SE	7083.9876, 2892.0258	5.3727, 1.8995	
	MEDIAN	13680.040	16.980	
	MIN, MAX	1152.194, 21077.996	9.217, 24.028	
	5%, 95%	1152.194, 21077.996	9.217, 24.028	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 146 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	748.939, 561.959		
	SD, SE	646.9264, 264.1066		
	MEDIAN	588.578		
	MIN, MAX	132.849, 2015.406		
	5%, 95%	132.849, 2015.406		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1185.202, 833.207		
	SD, SE	1099.5289, 448.8808		
	MEDIAN	723.589		
	MIN, MAX	232.042, 3148.998		
	5%, 95%	232.042, 3148.998		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1052.329, 571.033		
	SD, SE	1013.2672, 453.1469		
	MEDIAN	642.280		
	MIN, MAX	56.511, 2541.121		
	5%, 95%	56.511, 2541.121		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	976.310, 695.682		
	SD, SE	786.1268, 320.9349		
	MEDIAN	660.795		
	MIN, MAX	140.467, 2099.895		
	5%, 95%	140.467, 2099.895		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	5	0.0080
	MEAN, GEO MEAN	9.727, 6.689	0.013, 0.012	
	SD, SE	6.1408, 2.5070	0.0070, 0.0031	
	MEDIAN	10.503	0.012	
	MIN, MAX	0.656, 16.992	0.007, 0.025	
	5%, 95%	0.656, 16.992	0.007, 0.025	
Week 2	# of BLQ/ALQ Values	0/0	5/0	0.0034
	N	6	7	
	MEAN, GEO MEAN	10.292, 8.664	0.013, 0.011	
	SD, SE	5.4364, 2.2194	0.0079, 0.0030	
	MEDIAN	11.178	0.010	
	MIN, MAX	2.423, 17.741	0.005, 0.028	
Week 3	5%, 95%	2.423, 17.741	0.005, 0.028	0.0078
	# of BLQ/ALQ Values	0/0	7/0	
	N	5	6	
	MEAN, GEO MEAN	9.621, 6.094	0.013, 0.013	
	SD, SE	6.5461, 2.9275	0.0037, 0.0015	
	MEDIAN	12.366	0.015	
Overall ^b	MIN, MAX	0.605, 15.637	0.008, 0.016	0.0024
	5%, 95%	0.605, 15.637	0.008, 0.016	
	# of BLQ/ALQ Values	0/0	6/0	
	N	6	8	
	MEAN, GEO MEAN	9.857, 7.519	0.014, 0.013	
	SD, SE	5.7580, 2.3507	0.0055, 0.0019	
	MEDIAN	11.042	0.013	
	MIN, MAX	1.228, 16.790	0.007, 0.022	
	5%, 95%	1.228, 16.790	0.007, 0.022	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	0.543, 0.407	
	SD, SE	0.4628, 0.1889	
	MEDIAN	0.392	
	MIN, MAX	0.109, 1.416	
	5%, 95%	0.109, 1.416	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	0.888, 0.656	
	SD, SE	0.7346, 0.2999	
	MEDIAN	0.592	
	MIN, MAX	0.242, 1.993	
	5%, 95%	0.242, 1.993	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	0.945, 0.558	
	SD, SE	0.9479, 0.4239	
	MEDIAN	0.618	
	MIN, MAX	0.101, 2.427	
	5%, 95%	0.101, 2.427	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	0.764, 0.553	
	SD, SE	0.6189, 0.2527	
	MEDIAN	0.539	
	MIN, MAX	0.151, 1.618	
	5%, 95%	0.151, 1.618	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439020

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 149 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	5	0.0055
	MEAN, GEO MEAN	9217.7, 5485.6	7.9, 7.9	
	SD, SE	9594.01, 3916.74	0.00, 0.00	
	MEDIAN	7145.9	7.9	
	MIN, MAX	586.1, 27798.7	7.9, 7.9	
	5%, 95%	586.1, 27798.7	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	5/0	
Week 2	N	6	7	0.0015
	MEAN, GEO MEAN	9311.5, 6525.5	7.9, 7.9	
	SD, SE	7584.50, 3096.36	0.00, 0.00	
	MEDIAN	6886.9	7.9	
	MIN, MAX	1282.0, 21164.8	7.9, 7.9	
	5%, 95%	1282.0, 21164.8	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	6	0.0039
	MEAN, GEO MEAN	5950.2, 3511.4	7.9, 7.9	
	SD, SE	4438.14, 1984.80	0.00, 0.00	
	MEDIAN	5243.1	7.9	
	MIN, MAX	245.7, 12494.1	7.9, 7.9	
	5%, 95%	245.7, 12494.1	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	6/0	
Overall ^b	N	6	8	0.0008
	MEAN, GEO MEAN	8503.8, 5651.7	7.9, 7.9	
	SD, SE	7002.82, 2858.89	0.00, 0.00	
	MEDIAN	6639.0	7.9	
	MIN, MAX	704.6, 20485.9	7.9, 7.9	
	5%, 95%	704.6, 20485.9	7.9, 7.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 150 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	595.8, 333.9		
	SD, SE	849.24, 346.70		
	MEDIAN	293.4		
	MIN, MAX	97.7, 2316.6		
	5%, 95%	97.7, 2316.6		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	791.5, 494.5		
	SD, SE	749.41, 305.95		
	MEDIAN	510.7		
	MIN, MAX	128.2, 1924.1		
	5%, 95%	128.2, 1924.1		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	557.2, 321.5		
	SD, SE	516.34, 230.92		
	MEDIAN	262.2		
	MIN, MAX	41.0, 1181.9		
	5%, 95%	41.0, 1181.9		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	649.3, 419.5		
	SD, SE	628.04, 256.40		
	MEDIAN	430.3		
	MIN, MAX	89.0, 1760.6		
	5%, 95%	89.0, 1760.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 151 of 264)

Biomarker: NNAL (pg/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	149728.625, 135488.373	17892.457, 15800.916	
	SD, SE	67405.5472, 33702.7736	9736.3366, 3679.9893	
	MEDIAN	159918.500	12688.000	
	MIN, MAX	62452.500, 216625.000	8112.000, 33363.200	
	5%, 95%	62452.500, 216625.000	8112.000, 33363.200	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0106
	MEAN, GEO MEAN	197474.000, 185687.328	20190.857, 18701.256	
	SD, SE	75490.3263, 37745.1631	7792.0061, 2945.1015	
	MEDIAN	197263.000	21320.000	
	MIN, MAX	105754.000, 289616.000	7800.000, 33280.000	
	5%, 95%	105754.000, 289616.000	7800.000, 33280.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0107
	MEAN, GEO MEAN	173601.313, 161533.445	19041.657, 17423.551	
	SD, SE	67681.6128, 33840.8064	8398.6587, 3174.3946	
	MEDIAN	186319.000	17160.000	
	MIN, MAX	84103.250, 237664.000	7956.000, 33321.600	
	5%, 95%	84103.250, 237664.000	7956.000, 33321.600	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 152 of 264)

Biomarker: NNAL (pmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	715.703, 647.635	85.526, 75.528	
	SD, SE	322.1986, 161.0993	46.5396, 17.5903	
	MEDIAN	764.411	60.649	
	MIN, MAX	298.523, 1035.468	38.775, 159.476	
	5%, 95%	298.523, 1035.468	38.775, 159.476	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0106
	MEAN, GEO MEAN	943.926, 887.585	96.512, 89.392	
	SD, SE	360.8436, 180.4218	37.2457, 14.0776	
	MEDIAN	942.918	101.910	
	MIN, MAX	505.504, 1384.364	37.284, 159.078	
	5%, 95%	505.504, 1384.364	37.284, 159.078	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	4	7	0.0107
	MEAN, GEO MEAN	829.815, 772.130	91.019, 83.285	
	SD, SE	323.5181, 161.7590	40.1454, 15.1735	
	MEDIAN	890.606	82.025	
	MIN, MAX	402.014, 1136.034	38.030, 159.277	
	5%, 95%	402.014, 1136.034	38.030, 159.277	

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 153 of 264)

Biomarker: NNAL ((pg/24hr/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	4	
	MEAN, GEO MEAN	10190.435, 8614.184	
	SD, SE	6353.7672, 3176.8836	
	MEDIAN	9360.478	
	MIN, MAX	3469.583, 18571.200	
	5%, 95%	3469.583, 18571.200	
	# of BLQ/ALQ Values	0/0	
Week 3	N	4	
	MEAN, GEO MEAN	12847.485, 11279.740	
	SD, SE	7864.4053, 3932.2027	
	MEDIAN	10690.025	
	MIN, MAX	5875.222, 24134.667	
	5%, 95%	5875.222, 24134.667	
	# of BLQ/ALQ Values	0/0	
Overall*	N	4	
	MEAN, GEO MEAN	11518.960, 9998.806	
	SD, SE	7040.1168, 3520.0584	
	MEDIAN	10025.252	
	MIN, MAX	4672.403, 21352.934	
	5%, 95%	4672.403, 21352.934	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 154 of 264)

Biomarker: NNAL (pmol/24hr/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	4	
	MEAN, GEO MEAN	48.710, 41.176	
	SD, SE	30.3707, 15.1853	
	MEDIAN	44.743	
	MIN, MAX	16.585, 88.770	
	5%, 95%	16.585, 88.770	
	# of BLQ/ALQ Values	0/0	
Week 3	N	4	
	MEAN, GEO MEAN	61.411, 53.917	
	SD, SE	37.5918, 18.7959	
	MEDIAN	51.099	
	MIN, MAX	28.084, 115.364	
	5%, 95%	28.084, 115.364	
	# of BLQ/ALQ Values	0/0	
Overall*	N	4	
	MEAN, GEO MEAN	55.061, 47.795	
	SD, SE	33.6514, 16.8257	
	MEDIAN	47.921	
	MIN, MAX	22.335, 102.067	
	5%, 95%	22.335, 102.067	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 155 of 264)

Biomarker: NNAL (pg/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4	7	0.0182
	MEAN, GEO MEAN	130.848, 94.734	14.314, 10.611	
	SD, SE	114.7662, 57.3831	11.6080, 4.3874	
	MEDIAN	101.297	7.542	
	MIN, MAX	29.054, 291.743	3.645, 32.298	
	5%, 95%	29.054, 291.743	3.645, 32.298	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0107
	MEAN, GEO MEAN	133.676, 117.583	18.213, 13.362	
	SD, SE	77.0160, 38.5080	16.3222, 6.1692	
	MEDIAN	119.442	14.286	
	MIN, MAX	58.056, 237.764	3.741, 52.000	
	5%, 95%	58.056, 237.764	3.741, 52.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0107
	MEAN, GEO MEAN	132.262, 107.556	16.264, 12.155	
	SD, SE	95.8013, 47.9007	13.2303, 5.0006	
	MEDIAN	110.370	10.509	
	MIN, MAX	43.555, 264.754	3.693, 39.941	
	5%, 95%	43.555, 264.754	3.693, 39.941	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 156 of 264)

Biomarker: NNAL (pmol/mg Creatinine)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4	7	0.0182
	MEAN, GEO MEAN	0.626, 0.453	0.068, 0.050	
	SD, SE	0.5487, 0.2743	0.0555, 0.0210	
	MEDIAN	0.485	0.036	
	MIN, MAX	0.139, 1.395	0.017, 0.154	
	5%, 95%	0.139, 1.395	0.017, 0.154	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0107
	MEAN, GEO MEAN	0.639, 0.562	0.087, 0.064	
	SD, SE	0.3682, 0.1841	0.0782, 0.0296	
	MEDIAN	0.571	0.068	
	MIN, MAX	0.278, 1.137	0.018, 0.249	
	5%, 95%	0.278, 1.137	0.018, 0.249	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	4	7	0.0107
	MEAN, GEO MEAN	0.633, 0.515	0.078, 0.058	
	SD, SE	0.4579, 0.2289	0.0633, 0.0239	
	MEDIAN	0.528	0.050	
	MIN, MAX	0.209, 1.266	0.018, 0.191	
	5%, 95%	0.209, 1.266	0.018, 0.191	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 157 of 264)

Biomarker: NNAL (ng/mg Creatinine/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4		NA
	MEAN, GEO MEAN	10.392, 6.023		
	SD, SE	12.6764, 6.3382		
	MEDIAN	5.390		
	MIN, MAX	1.614, 29.174		
	5%, 95%	1.614, 29.174		
Week 3	# of BLQ/ALQ Values	0/0		NA
	N	4		
	MEAN, GEO MEAN	8.964, 7.143		
	SD, SE	7.4027, 3.7014		
	MEDIAN	6.409		
	MIN, MAX	3.225, 19.814		
Overall ^b	5%, 95%	3.225, 19.814		NA
	# of BLQ/ALQ Values	0/0		
	N	4		
	MEAN, GEO MEAN	9.679, 6.707		
	SD, SE	10.0346, 5.0173		
	MEDIAN	5.900		
	MIN, MAX	2.420, 24.494		
	5%, 95%	2.420, 24.494		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 158 of 264)

Biomarker: NNAL ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	4		NA
	MEAN, GEO MEAN	0.050, 0.029		
	SD, SE	0.0607, 0.0304		
	MEDIAN	0.026		
	MIN, MAX	0.008, 0.140		
	5%, 95%	0.008, 0.140		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	0.043, 0.034		
	SD, SE	0.0356, 0.0178		
	MEDIAN	0.031		
	MIN, MAX	0.015, 0.095		
	5%, 95%	0.015, 0.095		
	# of BLQ/ALQ Values	0/0		
Overall*	N	4		NA
	MEAN, GEO MEAN	0.047, 0.033		
	SD, SE	0.0482, 0.0241		
	MEDIAN	0.029		
	MIN, MAX	0.012, 0.118		
	5%, 95%	0.012, 0.118		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 159 of 264)

Biomarker: NNAL (pg/mL)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	122.8, 118.5	10.4, 10.4	
	SD, SE	38.17, 19.08	0.00, 0.00	
	MEDIAN	117.3	10.4	
	MIN, MAX	83.3, 173.3	10.4, 10.4	
	5%, 95%	83.3, 173.3	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0031
	MEAN, GEO MEAN	153.7, 127.2	10.4, 10.4	
	SD, SE	98.66, 49.33	0.00, 0.00	
	MEDIAN	142.5	10.4	
	MIN, MAX	46.0, 283.7	10.4, 10.4	
	5%, 95%	46.0, 283.7	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0031
	MEAN, GEO MEAN	138.2, 125.4	10.4, 10.4	
	SD, SE	68.33, 34.16	0.00, 0.00	
	MEDIAN	129.9	10.4	
	MIN, MAX	64.7, 228.5	10.4, 10.4	
	5%, 95%	64.7, 228.5	10.4, 10.4	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 160 of 264)

Biomarker: NNAL (pmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	586.9, 566.3	49.7, 49.7	
	SD, SE	182.44, 91.22	0.00, 0.00	
	MEDIAN	560.5	49.7	
	MIN, MAX	398.2, 828.4	49.7, 49.7	
	5%, 95%	398.2, 828.4	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0031
	MEAN, GEO MEAN	734.5, 608.1	49.7, 49.7	
	SD, SE	471.57, 235.79	0.00, 0.00	
	MEDIAN	681.0	49.7	
	MIN, MAX	219.9, 1356.1	49.7, 49.7	
	5%, 95%	219.9, 1356.1	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0031
	MEAN, GEO MEAN	660.7, 599.2	49.7, 49.7	
	SD, SE	326.69, 163.35	0.00, 0.00	
	MEDIAN	620.7	49.7	
	MIN, MAX	309.1, 1092.3	49.7, 49.7	
	5%, 95%	309.1, 1092.3	49.7, 49.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 161 of 264)

Biomarker: NNAL ((pg/mL)/cigarette per day)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4		NA
	MEAN, GEO MEAN	8.1, 7.5		
	SD, SE	3.51, 1.76		
	MEDIAN	7.5		
	MIN, MAX	4.6, 12.7		
	5%, 95%	4.6, 12.7		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	9.4, 7.8		
	SD, SE	5.37, 2.69		
	MEDIAN	10.3		
	MIN, MAX	2.6, 14.2		
	5%, 95%	2.6, 14.2		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	8.7, 7.8		
	SD, SE	4.27, 2.14		
	MEDIAN	9.2		
	MIN, MAX	3.6, 12.9		
	5%, 95%	3.6, 12.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 162 of 264)

Biomarker: NNAL ((pmol/L)/cigarette per day)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4		NA
	MEAN, GEO MEAN	38.6, 36.0		
	SD, SE	16.77, 8.38		
	MEDIAN	35.8		
	MIN, MAX	22.1, 60.8		
	5%, 95%	22.1, 60.8		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	44.7, 36.9		
	SD, SE	25.76, 12.88		
	MEDIAN	49.3		
	MIN, MAX	12.2, 67.8		
	5%, 95%	12.2, 67.8		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	4		NA
	MEAN, GEO MEAN	41.7, 37.2		
	SD, SE	20.37, 10.18		
	MEDIAN	43.9		
	MIN, MAX	17.2, 61.8		
	5%, 95%	17.2, 61.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 163 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	549554.500, 462813.558	17892.457, 15800.916	
	SD, SE	293611.7770, 146805.8885	9736.3366, 3679.9893	
	MEDIAN	604996.500	12688.000	
	MIN, MAX	152850.000, 835375.000	8112.000, 33363.200	
	5%, 95%	152850.000, 835375.000	8112.000, 33363.200	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0084
	MEAN, GEO MEAN	585318.250, 569775.116	23637.250, 21026.751	
	SD, SE	157681.1304, 78840.5652	12126.9421, 4287.5215	
	MEDIAN	566380.500	21580.000	
	MIN, MAX	413080.000, 795432.000	7800.000, 47762.000	
	5%, 95%	413080.000, 795432.000	7800.000, 47762.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0085
	MEAN, GEO MEAN	567436.375, 535070.239	22631.700, 19764.230	
	SD, SE	191729.1352, 95864.5676	12789.3686, 4521.7246	
	MEDIAN	644308.500	19552.000	
	MIN, MAX	282965.000, 698163.500	7956.000, 47762.000	
	5%, 95%	282965.000, 698163.500	7956.000, 47762.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 164 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/24hr) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	2626.871, 2212.249	85.526, 75.528	
	SD, SE	1403.4645, 701.7323	46.5396, 17.5903	
	MEDIAN	2891.884	60.649	
	MIN, MAX	730.623, 3993.093	38.775, 159.476	
	5%, 95%	730.623, 3993.093	38.775, 159.476	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0084
	MEAN, GEO MEAN	2797.821, 2723.525	112.986, 100.508	
	SD, SE	753.7159, 376.8580	57.9667, 20.4943	
	MEDIAN	2707.299	103.153	
	MIN, MAX	1974.522, 3802.165	37.284, 228.302	
	5%, 95%	1974.522, 3802.165	37.284, 228.302	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0085
	MEAN, GEO MEAN	2712.346, 2557.636	108.180, 94.473	
	SD, SE	916.4653, 458.2327	61.1329, 21.6138	
	MEDIAN	3079.795	93.459	
	MIN, MAX	1352.573, 3337.222	38.030, 228.302	
	5%, 95%	1352.573, 3337.222	38.030, 228.302	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439036

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 165 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4		NA
	MEAN, GEO MEAN	36071.731, 29425.119		
	SD, SE	19984.6413, 9992.3206		
	MEDIAN	41741.728		
	MIN, MAX	8491.667, 52311.800		
	5%, 95%	8491.667, 52311.800		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	37705.629, 34611.491		
	SD, SE	19492.3489, 9746.1745		
	MEDIAN	30793.813		
	MIN, MAX	22948.889, 66286.000		
	5%, 95%	22948.889, 66286.000		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	36888.680, 33129.734		
	SD, SE	18231.6861, 9115.8431		
	MEDIAN	36267.771		
	MIN, MAX	15720.278, 59298.900		
	5%, 95%	15720.278, 59298.900		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439037

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 166 of 264)

Biomarker: NNAL plus NNAL-gluc ((pmol/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4		NA
	MEAN, GEO MEAN	172.423, 140.652		
	SD, SE	95.5266, 47.7633		
	MEDIAN	199.526		
	MIN, MAX	40.590, 250.050		
	5%, 95%	40.590, 250.050		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	180.233, 165.443		
	SD, SE	93.1733, 46.5867		
	MEDIAN	147.195		
	MIN, MAX	109.696, 316.847		
	5%, 95%	109.696, 316.847		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	176.328, 158.360		
	SD, SE	87.1476, 43.5738		
	MEDIAN	173.361		
	MIN, MAX	75.143, 283.449		
	5%, 95%	75.143, 283.449		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439038

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 167 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	440.191, 323.602	14.314, 10.611	
	SD, SE	307.2483, 153.6242	11.6080, 4.3874	
	MEDIAN	433.932	7.542	
	MIN, MAX	71.110, 821.789	3.645, 32.298	
	5%, 95%	71.110, 821.789	3.645, 32.298	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0085
	MEAN, GEO MEAN	390.576, 360.799	19.274, 14.570	
	SD, SE	186.7461, 93.3730	15.4065, 5.4470	
	MEDIAN	341.258	15.795	
	MIN, MAX	226.768, 653.021	3.741, 52.000	
	5%, 95%	226.768, 653.021	3.741, 52.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0085
	MEAN, GEO MEAN	415.384, 358.342	17.569, 13.411	
	SD, SE	242.5057, 121.2529	12.7926, 4.5229	
	MEDIAN	387.595	13.741	
	MIN, MAX	148.939, 737.405	3.693, 39.941	
	5%, 95%	148.939, 737.405	3.693, 39.941	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 168 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4	7	0.0107
	MEAN, GEO MEAN	2.104, 1.547	0.068, 0.050	
	SD, SE	1.4686, 0.7343	0.0555, 0.0210	
	MEDIAN	2.075	0.036	
	MIN, MAX	0.340, 3.928	0.017, 0.154	
	5%, 95%	0.340, 3.928	0.017, 0.154	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0085
	MEAN, GEO MEAN	1.867, 1.724	0.092, 0.070	
	SD, SE	0.8925, 0.4462	0.0739, 0.0261	
	MEDIAN	1.631	0.076	
	MIN, MAX	1.084, 3.121	0.018, 0.249	
	5%, 95%	1.084, 3.121	0.018, 0.249	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0085
	MEAN, GEO MEAN	1.986, 1.713	0.084, 0.064	
	SD, SE	1.1592, 0.5796	0.0612, 0.0217	
	MEDIAN	1.853	0.066	
	MIN, MAX	0.712, 3.525	0.018, 0.191	
	5%, 95%	0.712, 3.525	0.018, 0.191	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439040

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 169 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4		NA
	MEAN, GEO MEAN	33.394, 20.575		
	SD, SE	33.9393, 16.9697		
	MEDIAN	23.723		
	MIN, MAX	3.951, 82.179		
	5%, 95%	3.951, 82.179		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	25.939, 21.917		
	SD, SE	19.1954, 9.5977		
	MEDIAN	18.370		
	MIN, MAX	12.598, 54.418		
	5%, 95%	12.598, 54.418		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	29.667, 22.351		
	SD, SE	26.4666, 13.2333		
	MEDIAN	21.047		
	MIN, MAX	8.275, 68.299		
	5%, 95%	8.275, 68.299		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 170 of 264)

Biomarker: NNAL plus NNAL plus ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4		NA
	MEAN, GEO MEAN	0.160, 0.099		
	SD, SE	0.1622, 0.0811		
	MEDIAN	0.114		
	MIN, MAX	0.019, 0.393		
	5%, 95%	0.019, 0.393		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	0.124, 0.104		
	SD, SE	0.0918, 0.0459		
	MEDIAN	0.088		
	MIN, MAX	0.060, 0.260		
	5%, 95%	0.060, 0.260		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	0.142, 0.107		
	SD, SE	0.1267, 0.0633		
	MEDIAN	0.101		
	MIN, MAX	0.040, 0.327		
	5%, 95%	0.040, 0.327		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 171 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mL)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	445.0, 404.7	10.4, 10.4	
	SD, SE	205.33, 102.66	0.00, 0.00	
	MEDIAN	453.9	10.4	
	MIN, MAX	203.8, 668.3	10.4, 10.4	
	5%, 95%	203.8, 668.3	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0033
	MEAN, GEO MEAN	444.2, 390.3	13.7, 12.2	
	SD, SE	251.04, 125.52	9.30, 3.29	
	MEDIAN	407.0	10.4	
	MIN, MAX	179.6, 783.3	10.4, 36.7	
	5%, 95%	179.6, 783.3	10.4, 36.7	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0033
	MEAN, GEO MEAN	444.6, 403.5	13.7, 12.2	
	SD, SE	201.70, 100.85	9.30, 3.29	
	MEDIAN	460.2	10.4	
	MIN, MAX	191.7, 666.4	10.4, 36.7	
	5%, 95%	191.7, 666.4	10.4, 36.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 172 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	2127.0, 1934.3	49.7, 49.7	
	SD, SE	981.45, 490.73	0.00, 0.00	
	MEDIAN	2169.7	49.7	
	MIN, MAX	974.2, 3194.5	49.7, 49.7	
	5%, 95%	974.2, 3194.5	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	8	0.0033
	MEAN, GEO MEAN	2123.3, 1865.7	65.4, 58.2	
	SD, SE	1199.98, 599.99	44.44, 15.71	
	MEDIAN	1945.2	49.7	
	MIN, MAX	858.5, 3744.2	49.7, 175.4	
	5%, 95%	858.5, 3744.2	49.7, 175.4	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	8	0.0033
	MEAN, GEO MEAN	2125.2, 1928.8	65.4, 58.2	
	SD, SE	964.06, 482.03	44.44, 15.71	
	MEDIAN	2199.5	49.7	
	MIN, MAX	916.4, 3185.4	49.7, 175.4	
	5%, 95%	916.4, 3185.4	49.7, 175.4	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 173 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/mL)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	4	
	MEAN, GEO MEAN	28.5, 25.7	
	SD, SE	12.47, 6.24	
	MEDIAN	31.7	
	MIN, MAX	11.3, 39.3	
	5%, 95%	11.3, 39.3	
	# of BLQ/ALQ Values	0/0	
Week 3	N	4	
	MEAN, GEO MEAN	26.9, 23.7	
	SD, SE	13.42, 6.71	
	MEDIAN	29.2	
	MIN, MAX	10.0, 39.2	
	5%, 95%	10.0, 39.2	
	# of BLQ/ALQ Values	0/0	
Overall*	N	4	
	MEAN, GEO MEAN	27.7, 25.1	
	SD, SE	11.53, 5.77	
	MEDIAN	32.2	
	MIN, MAX	10.7, 35.9	
	5%, 95%	10.7, 35.9	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	4		NA
	MEAN, GEO MEAN	136.2, 123.0		
	SD, SE	59.64, 29.82		
	MEDIAN	151.3		
	MIN, MAX	54.1, 187.9		
	5%, 95%	54.1, 187.9		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	128.6, 113.3		
	SD, SE	64.12, 32.06		
	MEDIAN	139.8		
	MIN, MAX	47.7, 187.2		
	5%, 95%	47.7, 187.2		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	4		NA
	MEAN, GEO MEAN	132.4, 119.7		
	SD, SE	55.22, 27.61		
	MEDIAN	153.5		
	MIN, MAX	50.9, 171.8		
	5%, 95%	50.9, 171.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 175 of 264)

Biomarker: NNAL-O-glucuronide (pmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	1540.2, 1323.6	0.0, NA	
	SD, SE	910.77, 455.39	0.00, 0.00	
	MEDIAN	1451.5	0.0	
	MIN, MAX	576.1, 2681.6	0.0, 0.0	
	5%, 95%	576.1, 2681.6	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0031
	MEAN, GEO MEAN	1388.9, 1249.1	0.0, NA	
	SD, SE	729.66, 364.83	0.00, 0.00	
	MEDIAN	1264.3	0.0	
	MIN, MAX	638.7, 2388.1	0.0, 0.0	
	5%, 95%	638.7, 2388.1	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0031
	MEAN, GEO MEAN	1464.5, 1315.6	0.0, NA	
	SD, SE	690.13, 345.06	0.00, 0.00	
	MEDIAN	1578.8	0.0	
	MIN, MAX	607.4, 2093.2	0.0, 0.0	
	5%, 95%	607.4, 2093.2	0.0, 0.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 176 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/L)/cigarette per day) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4		NA
	MEAN, GEO MEAN	97.5, 84.1		
	SD, SE	52.09, 26.05		
	MEDIAN	100.2		
	MIN, MAX	32.0, 157.7		
	5%, 95%	32.0, 157.7		
	# of BLQ/ALQ Values	0/0		
Week 3	N	4		NA
	MEAN, GEO MEAN	84.0, 75.9		
	SD, SE	38.36, 19.18		
	MEDIAN	90.5		
	MIN, MAX	35.5, 119.4		
	5%, 95%	35.5, 119.4		
	# of BLQ/ALQ Values	0/0		
Overall ^a	N	4		NA
	MEAN, GEO MEAN	90.8, 81.7		
	SD, SE	38.20, 19.10		
	MEDIAN	107.4		
	MIN, MAX	33.8, 114.6		
	5%, 95%	33.8, 114.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 177 of 264)

Biomarker: NNAL-O-glucuronide (pmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	1911.172, 1513.743	0.000, NA	
	SD, SE	1220.1075, 610.0537	0.0000, 0.0000	
	MEDIAN	1930.306	0.000	
	MIN, MAX	432.075, 3352.000	0.000, 0.000	
	5%, 95%	432.075, 3352.000	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0031
	MEAN, GEO MEAN	1853.886, 1823.438	0.000, NA	
	SD, SE	401.2446, 200.6223	0.0000, 0.0000	
	MEDIAN	1764.388	0.000	
	MIN, MAX	1469.010, 2417.760	0.000, 0.000	
	5%, 95%	1469.010, 2417.760	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	4	7	0.0031
	MEAN, GEO MEAN	1882.529, 1770.202	0.000, NA	
	SD, SE	675.7396, 337.8698	0.0000, 0.0000	
	MEDIAN	2005.422	0.000	
	MIN, MAX	950.543, 2568.731	0.000, 0.000	
	5%, 95%	950.543, 2568.731	0.000, 0.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 178 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	4	NA
	MEAN, GEO MEAN	123.714, 96.242	
	SD, SE	75.0082, 37.5041	
	MEDIAN	136.837	
	MIN, MAX	24.004, 197.176	
	5%, 95%	24.004, 197.176	
Week 3	# of BLQ/ALQ Values	0/0	
	N	4	NA
	MEAN, GEO MEAN	118.821, 110.767	
	SD, SE	56.0040, 28.0020	
	MEDIAN	96.097	
	MIN, MAX	81.612, 201.480	
Overall*	5%, 95%	81.612, 201.480	
	# of BLQ/ALQ Values	0/0	
	N	4	NA
	MEAN, GEO MEAN	121.268, 109.622	
	SD, SE	56.7231, 28.3615	
	MEDIAN	125.440	
	MIN, MAX	52.808, 181.383	
	5%, 95%	52.808, 181.383	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 179 of 264)

Biomarker: NNAL-O-glucuronide (pmol/mg Creatinine)		Analytical Lab: TNBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	4	7	0.0031
	MEAN, GEO MEAN	1.479, 1.058	0.000, NA	
	SD, SE	0.9830, 0.4915	0.0000, 0.0000	
	MEDIAN	1.590	0.000	
	MIN, MAX	0.201, 2.534	0.000, 0.000	
	5%, 95%	0.201, 2.534	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	4	7	0.0031
	MEAN, GEO MEAN	1.228, 1.155	0.000, NA	
	SD, SE	0.5275, 0.2638	0.0000, 0.0000	
	MEDIAN	1.061	0.000	
	MIN, MAX	0.806, 1.985	0.000, 0.000	
	5%, 95%	0.806, 1.985	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	4	7	0.0031
	MEAN, GEO MEAN	1.354, 1.189	0.000, NA	
	SD, SE	0.7197, 0.3599	0.0000, 0.0000	
	MEDIAN	1.326	0.000	
	MIN, MAX	0.504, 2.260	0.000, 0.000	
	5%, 95%	0.504, 2.260	0.000, 0.000	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 180 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/mg Creatinine)/cigarette per day). Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	4	
	MEAN, GEO MEAN	0.110, 0.067	
	SD, SE	0.1034, 0.0517	
	MEDIAN	0.088	
	MIN, MAX	0.011, 0.253	
	5%, 95%	0.011, 0.253	
	# of BLQ/ALQ Values	0/0	
Week 3	N	4	
	MEAN, GEO MEAN	0.081, 0.070	
	SD, SE	0.0563, 0.0282	
	MEDIAN	0.057	
	MIN, MAX	0.045, 0.165	
	5%, 95%	0.045, 0.165	
	# of BLQ/ALQ Values	0/0	
Overall*	N	4	
	MEAN, GEO MEAN	0.096, 0.074	
	SD, SE	0.0789, 0.0395	
	MEDIAN	0.073	
	MIN, MAX	0.028, 0.209	
	5%, 95%	0.028, 0.209	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 181 of 264)

Biomarker: Nicotine (nmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	9618.834, 7479.916	7.072, 6.609	
	SD, SE	7409.9864, 3025.1143	3.0623, 1.7680	
	MEDIAN	6290.338	6.936	
	MIN, MAX	3259.536, 19895.897	4.080, 10.200	
	5%, 95%	3259.536, 19895.897	4.080, 10.200	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	8208.238, 7076.088	7.548, 6.393	
	SD, SE	4490.9820, 1833.4357	5.6738, 4.0120	
	MEDIAN	8354.878	7.548	
	MIN, MAX	3484.431, 13388.466	3.536, 11.560	
	5%, 95%	3484.431, 13388.466	3.536, 11.560	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	6005.220, 5280.694	7.076, 6.689	
	SD, SE	2926.7725, 1308.8925	2.7799, 1.3899	
	MEDIAN	7103.308	6.569	
	MIN, MAX	2126.580, 8844.885	4.284, 10.880	
	5%, 95%	2126.580, 8844.885	4.284, 10.880	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0051
	MEAN, GEO MEAN	8471.514, 7224.185	8.359, 7.845	
	SD, SE	5060.2532, 2065.8397	2.9810, 1.2170	
	MEDIAN	7066.450	8.609	
	MIN, MAX	3555.830, 15498.722	3.967, 11.560	
	5%, 95%	3555.830, 15498.722	3.967, 11.560	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 182 of 264)

Biomarker: Nicotine (ng/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	1560.175, 1213.243	1.147, 1.072	
	SD, SE	1201.8996, 490.6734	0.4964, 0.2866	
	MEDIAN	1020.293	1.125	
	MIN, MAX	528.697, 3227.114	0.662, 1.654	
	5%, 95%	528.697, 3227.114	0.662, 1.654	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	1331.376, 1147.742	1.225, 1.037	
	SD, SE	728.4371, 297.3832	0.9199, 0.6505	
	MEDIAN	1355.162	1.225	
	MIN, MAX	565.175, 2171.609	0.574, 1.875	
	5%, 95%	565.175, 2171.609	0.574, 1.875	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	974.047, 856.528	1.148, 1.085	
	SD, SE	474.7226, 212.3024	0.4509, 0.2255	
	MEDIAN	1152.157	1.066	
	MIN, MAX	344.931, 1434.640	0.695, 1.765	
	5%, 95%	344.931, 1434.640	0.695, 1.765	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0051
	MEAN, GEO MEAN	1374.080, 1171.763	1.356, 1.273	
	SD, SE	820.7730, 335.0792	0.4833, 0.1973	
	MEDIAN	1146.178	1.396	
	MIN, MAX	576.756, 2513.893	0.644, 1.875	
	5%, 95%	576.756, 2513.893	0.644, 1.875	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 183 of 264)

Biomarker: Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	636.191, 455.251		
	SD, SE	531.8371, 217.1216		
	MEDIAN	535.377		
	MIN, MAX	181.085, 1503.563		
	5%, 95%	181.085, 1503.563		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	765.869, 536.234		
	SD, SE	716.1272, 292.3577		
	MEDIAN	451.760		
	MIN, MAX	178.705, 2015.446		
	5%, 95%	178.705, 2015.446		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	618.861, 483.430		
	SD, SE	510.4448, 228.2779		
	MEDIAN	394.628		
	MIN, MAX	187.266, 1474.148		
	5%, 95%	187.266, 1474.148		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	678.707, 553.168		
	SD, SE	433.9425, 177.1563		
	MEDIAN	612.633		
	MIN, MAX	221.461, 1239.200		
	5%, 95%	221.461, 1239.200		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((ug/24hr/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	103.190, 73.842	
	SD, SE	86.2639, 35.2171	
	MEDIAN	86.839	
	MIN, MAX	29.372, 243.878	
	5%, 95%	29.372, 243.878	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	
	MEAN, GEO MEAN	124.224, 86.977	
	SD, SE	116.1556, 47.4203	
	MEDIAN	73.276	
	MIN, MAX	28.986, 326.905	
	5%, 95%	28.986, 326.905	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	
	MEAN, GEO MEAN	100.380, 78.413	
	SD, SE	82.7940, 37.0266	
	MEDIAN	64.009	
	MIN, MAX	30.375, 239.107	
	5%, 95%	30.375, 239.107	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	
	MEAN, GEO MEAN	110.087, 89.724	
	SD, SE	70.3855, 28.7347	
	MEDIAN	99.370	
	MIN, MAX	35.921, 200.998	
	5%, 95%	35.921, 200.998	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	3	0.0275
	MEAN, GEO MEAN	6.631, 5.419	0.005, 0.005	
	SD, SE	4.3231, 1.7649	0.0006, 0.0003	
	MEDIAN	5.003	0.005	
	MIN, MAX	1.717, 12.677	0.004, 0.005	
	5%, 95%	1.717, 12.677	0.004, 0.005	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	6.414, 5.576	0.008, 0.006	
	SD, SE	3.4787, 1.4202	0.0064, 0.0045	
	MEDIAN	6.483	0.008	
	MIN, MAX	2.159, 12.067	0.003, 0.012	
	5%, 95%	2.159, 12.067	0.003, 0.012	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	5.449, 5.159	0.006, 0.005	
	SD, SE	2.0593, 0.9210	0.0024, 0.0012	
	MEDIAN	4.773	0.006	
	MIN, MAX	3.605, 8.447	0.003, 0.008	
	5%, 95%	3.605, 8.447	0.003, 0.008	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0050
	MEAN, GEO MEAN	6.376, 5.742	0.006, 0.006	
	SD, SE	3.0639, 1.2508	0.0032, 0.0013	
	MEDIAN	5.903	0.005	
	MIN, MAX	2.883, 10.457	0.004, 0.012	
	5%, 95%	2.883, 10.457	0.004, 0.012	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (µg/mg Creatinine)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0256
	MEAN, GEO MEAN	1.076, 0.879	0.001, 0.001	
	SD, SE	0.7014, 0.2863	0.0000, 0.0000	
	MEDIAN	0.812	0.001	
	MIN, MAX	0.278, 2.056	0.001, 0.001	
	5%, 95%	0.278, 2.056	0.001, 0.001	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	1.040, 0.904	0.001, NA	
	SD, SE	0.5642, 0.2303	0.0014, 0.0010	
	MEDIAN	1.052	0.001	
	MIN, MAX	0.350, 1.957	0.000, 0.002	
	5%, 95%	0.350, 1.957	0.000, 0.002	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0179
	MEAN, GEO MEAN	0.884, 0.837	0.001, NA	
	SD, SE	0.3339, 0.1493	0.0005, 0.0003	
	MEDIAN	0.774	0.001	
	MIN, MAX	0.585, 1.370	0.000, 0.001	
	5%, 95%	0.585, 1.370	0.000, 0.001	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0043
	MEAN, GEO MEAN	1.034, 0.931	0.001, NA	
	SD, SE	0.4971, 0.2029	0.0006, 0.0003	
	MEDIAN	0.958	0.001	
	MIN, MAX	0.467, 1.696	0.000, 0.002	
	5%, 95%	0.467, 1.696	0.000, 0.002	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., "<1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6		NA
	MEAN, GEO MEAN	0.455, 0.329		
	SD, SE	0.3700, 0.1511		
	MEDIAN	0.360		
	MIN, MAX	0.095, 1.056		
	5%, 95%	0.095, 1.056		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.582, 0.423		
	SD, SE	0.4804, 0.1961		
	MEDIAN	0.364		
	MIN, MAX	0.108, 1.275		
	5%, 95%	0.108, 1.275		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.608, 0.472		
	SD, SE	0.4860, 0.2173		
	MEDIAN	0.552		
	MIN, MAX	0.180, 1.408		
	5%, 95%	0.180, 1.408		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.538, 0.442		
	SD, SE	0.3327, 0.1358		
	MEDIAN	0.495		
	MIN, MAX	0.156, 0.948		
	5%, 95%	0.156, 0.948		
	# of BLQ/ALQ Values	0/0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((ug/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.074, 0.053		
	SD, SE	0.0601, 0.0245		
	MEDIAN	0.059		
	MIN, MAX	0.015, 0.171		
	5%, 95%	0.015, 0.171		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.095, 0.069		
	SD, SE	0.0779, 0.0318		
	MEDIAN	0.059		
	MIN, MAX	0.018, 0.207		
	5%, 95%	0.018, 0.207		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.099, 0.077		
	SD, SE	0.0787, 0.0352		
	MEDIAN	0.090		
	MIN, MAX	0.029, 0.228		
	5%, 95%	0.029, 0.228		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.087, 0.072		
	SD, SE	0.0540, 0.0220		
	MEDIAN	0.081		
	MIN, MAX	0.025, 0.154		
	5%, 95%	0.025, 0.154		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker, Trans-3-hydroxycotinine (ng/mL)	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	3549.7, 2312.1	44, 2.2	
	SD, SE	3173.27, 448.77	9.97, 1.24	
	MEDIAN	3110.5	1.4	
	MIN, MAX	30.1, 17333.8	1.0, 77.2	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	4688.4, 3050.3	62, 2.4	
	SD, SE	3986.05, 569.44	17.70, 2.19	
	MEDIAN	3435.7	1.7	
	MIN, MAX	26.9, 18865.3	1.0, 135.0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	3636.9, 2545.4	3.6, 2.0	
	SD, SE	2820.50, 415.86	7.31, 0.91	
	MEDIAN	3045.4	1.3	
	MIN, MAX	20.4, 15599.2	1.0, 56.0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3928.4, 2775.7	4.7, 2.4	
	SD, SE	2928.37, 414.13	9.29, 1.15	
	MEDIAN	3463.0	1.8	
	MIN, MAX	25.8, 13970.9	1.0, 52.6	
# of BLQ/ALQ Values		0/0	1.0, 14.3	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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PM3006438995

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 190 of 264)

Biomarker: Nicotine (ng/mL)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	3	0.0256
	MEAN, GEO MEAN	1167.4, 720.8	0.6, 0.6	
	SD, SE	1258.24, 513.67	0.00, 0.00	
	MEDIAN	550.6	0.6	
	MIN, MAX	220.0, 3363.8	0.6, 0.6	
	5%, 95%	220.0, 3363.8	0.6, 0.6	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	2	0.0631
	MEAN, GEO MEAN	982.4, 681.2	0.6, 0.6	
	SD, SE	874.12, 356.86	0.00, 0.00	
	MEDIAN	612.3	0.6	
	MIN, MAX	292.8, 2335.1	0.6, 0.6	
	5%, 95%	292.8, 2335.1	0.6, 0.6	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0151
	MEAN, GEO MEAN	551.6, 482.2	0.6, 0.6	
	SD, SE	284.63, 127.29	0.00, 0.00	
	MEDIAN	667.3	0.6	
	MIN, MAX	248.0, 858.7	0.6, 0.6	
	5%, 95%	248.0, 858.7	0.6, 0.6	
	# of BLQ/ALQ Values	0/0	4/0	
Overall*	N	6	6	0.0028
	MEAN, GEO MEAN	974.0, 707.3	0.6, 0.6	
	SD, SE	836.80, 341.62	0.00, 0.00	
	MEDIAN	569.9	0.6	
	MIN, MAX	253.8, 2185.9	0.6, 0.6	
	5%, 95%	253.8, 2185.9	0.6, 0.6	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 191 of 264)

Biomarker: Nicotine (nmol/L/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	525.7, 270.5	
	SD, SE	636.62, 259.90	
	MEDIAN	322.6	
	MIN, MAX	67.8, 1728.2	
	5%, 95%	67.8, 1728.2	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	526.4, 318.3	
	SD, SE	504.53, 205.97	
	MEDIAN	365.7	
	MIN, MAX	90.3, 1308.7	
	5%, 95%	90.3, 1308.7	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	342.3, 272.1	
	SD, SE	231.29, 103.44	
	MEDIAN	256.8	
	MIN, MAX	76.4, 685.7	
	5%, 95%	76.4, 685.7	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	475.7, 337.9	
	SD, SE	389.64, 159.07	
	MEDIAN	447.2	
	MIN, MAX	78.2, 1159.4	
	5%, 95%	78.2, 1159.4	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 192 of 264)

Biomarker: Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6		NA
	MEAN, GEO MEAN	85.3, 43.9		
	SD, SE	103.25, 42.15		
	MEDIAN	52.3		
	MIN, MAX	11.0, 280.3		
	5%, 95%	11.0, 280.3		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	85.4, 51.6		
	SD, SE	81.86, 33.42		
	MEDIAN	59.3		
	MIN, MAX	14.6, 212.3		
	5%, 95%	14.6, 212.3		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	55.5, 44.2		
	SD, SE	37.50, 16.77		
	MEDIAN	41.7		
	MIN, MAX	12.4, 111.2		
	5%, 95%	12.4, 111.2		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	77.2, 54.8		
	SD, SE	63.21, 25.81		
	MEDIAN	72.6		
	MIN, MAX	12.7, 188.1		
	5%, 95%	12.7, 188.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 193 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/L)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0651
	MEAN, GEO MEAN	2601.8, 1698.4	9.3, 9.3	
	SD, SE	2910.33, 1188.14	0.00, 0.00	
	MEDIAN	1692.2	9.3	
	MIN, MAX	403.4, 8373.6	9.3, 9.3	
	5%, 95%	403.4, 8373.6	9.3, 9.3	
	# of BLQ/ALQ Values	0/0	2/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	2877.9, 2365.5	27.7, 20.7	
	SD, SE	2171.62, 886.56	25.95, 18.35	
	MEDIAN	2040.6	27.7	
	MIN, MAX	1145.6, 6965.8	9.3, 46.0	
	5%, 95%	1145.6, 6965.8	9.3, 46.0	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0151
	MEAN, GEO MEAN	1850.7, 1460.3	9.3, 9.3	
	SD, SE	1312.92, 587.16	0.00, 0.00	
	MEDIAN	1299.6	9.3	
	MIN, MAX	432.7, 3839.2	9.3, 9.3	
	5%, 95%	432.7, 3839.2	9.3, 9.3	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0037
	MEAN, GEO MEAN	2495.4, 1962.5	11.3, 10.7	
	SD, SE	2051.46, 837.50	4.98, 2.03	
	MEDIAN	1908.5	9.3	
	MIN, MAX	797.4, 6392.9	9.3, 21.5	
	5%, 95%	797.4, 6392.9	9.3, 21.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 194 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	175.8, 103.3		
	SD, SE	255.97, 104.50		
	MEDIAN	72.4		
	MIN, MAX	55.6, 697.8		
	5%, 95%	55.6, 697.8		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	251.7, 179.3		
	SD, SE	223.92, 91.42		
	MEDIAN	165.8		
	MIN, MAX	57.3, 633.3		
	5%, 95%	57.3, 633.3		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	185.7, 133.7		
	SD, SE	161.67, 72.30		
	MEDIAN	72.2		
	MIN, MAX	64.1, 400.1		
	5%, 95%	64.1, 400.1		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	201.4, 145.3		
	SD, SE	190.41, 77.73		
	MEDIAN	115.5		
	MIN, MAX	59.0, 550.3		
	5%, 95%	59.0, 550.3		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 195 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	3721.249, 2858.728	19.530, 17.646	
	SD, SE	2425.2308, 990.0963	11.8370, 8.3700	
	MEDIAN	3264.808	19.530	
	MIN, MAX	548.624, 7285.032	11.160, 27.900	
	5%, 95%	548.624, 7285.032	11.160, 27.900	
	# of BLQ/ALQ Values	0/0	2/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	4160.740, 3985.670	39.730, 38.893	
	SD, SE	1399.0642, 571.1656	11.4693, 8.1100	
	MEDIAN	3587.759	39.730	
	MIN, MAX	2816.360, 6478.194	31.620, 47.840	
	5%, 95%	2816.360, 6478.194	31.620, 47.840	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	3377.796, 2594.128	19.353, 18.296	
	SD, SE	2201.0589, 984.3435	7.6038, 3.8019	
	MEDIAN	3139.430	17.968	
	MIN, MAX	597.126, 5950.760	11.718, 29.760	
	5%, 95%	597.126, 5950.760	11.718, 29.760	
	# of BLQ/ALQ Values	0/0	4/0	
Overall [*]	N	6	6	0.0051
	MEAN, GEO MEAN	3758.070, 3321.287	24.798, 24.160	
	SD, SE	1913.2244, 781.0706	5.9768, 2.4400	
	MEDIAN	3384.818	25.737	
	MIN, MAX	1320.703, 6571.329	16.740, 31.620	
	5%, 95%	1320.703, 6571.329	16.740, 31.620	

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	216.883, 173.991	
	SD, SE	193.3379, 78.9299	
	MEDIAN	152.465	
	MIN, MAX	91.437, 607.086	
	5%, 95%	91.437, 607.086	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	
	MEAN, GEO MEAN	377.385, 302.039	
	SD, SE	290.7399, 118.6941	
	MEDIAN	231.422	
	MIN, MAX	163.182, 871.789	
	5%, 95%	163.182, 871.789	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	
	MEAN, GEO MEAN	345.192, 237.484	
	SD, SE	330.7153, 147.9004	
	MEDIAN	156.972	
	MIN, MAX	99.521, 860.215	
	5%, 95%	99.521, 860.215	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	
	MEAN, GEO MEAN	303.001, 242.313	
	SD, SE	231.0965, 94.3447	
	MEDIAN	163.854	
	MIN, MAX	133.616, 635.179	
	5%, 95%	133.616, 635.179	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	2.750, 2.071	0.013, 0.012	
	SD, SE	1.8455, 0.7534	0.0021, 0.0015	
	MEDIAN	2.837	0.013	
	MIN, MAX	0.452, 5.118	0.011, 0.014	
	5%, 95%	0.452, 5.118	0.011, 0.014	
	# of BLQ/ALQ Values	0/0	2/0	
Week 2	N	6	2	0.0668
	MEAN, GEO MEAN	3.341, 3.141	0.036, 0.036	
	SD, SE	1.3634, 0.5566	0.0042, 0.0030	
	MEDIAN	3.126	0.036	
	MIN, MAX	1.972, 5.839	0.033, 0.039	
	5%, 95%	1.972, 5.839	0.033, 0.039	
	# of BLQ/ALQ Values	0/0	2/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	3.039, 2.535	0.015, 0.014	
	SD, SE	1.8280, 0.8175	0.0059, 0.0029	
	MEDIAN	3.022	0.015	
	MIN, MAX	1.066, 4.929	0.009, 0.021	
	5%, 95%	1.066, 4.929	0.009, 0.021	
	# of BLQ/ALQ Values	0/0	4/0	
Overall ^b	N	6	6	0.0050
	MEAN, GEO MEAN	2.992, 2.662	0.019, 0.018	
	SD, SE	1.5386, 0.6281	0.0081, 0.0033	
	MEDIAN	2.800	0.020	
	MIN, MAX	1.486, 5.254	0.011, 0.033	
	5%, 95%	1.486, 5.254	0.011, 0.033	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.161, 0.126		
	SD, SE	0.1384, 0.0565		
	MEDIAN	0.103		
	MIN, MAX	0.066, 0.427		
	5%, 95%	0.066, 0.427		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.296, 0.238		
	SD, SE	0.2022, 0.0826		
	MEDIAN	0.238		
	MIN, MAX	0.099, 0.552		
	5%, 95%	0.099, 0.552		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.325, 0.232		
	SD, SE	0.3027, 0.1354		
	MEDIAN	0.178		
	MIN, MAX	0.076, 0.822		
	5%, 95%	0.076, 0.822		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.248, 0.196		
	SD, SE	0.1817, 0.0742		
	MEDIAN	0.178		
	MIN, MAX	0.080, 0.499		
	5%, 95%	0.080, 0.499		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	51.700, 44.630	0.084, 0.078	
	SD, SE	29.5718, 12.0726	0.0403, 0.0285	
	MEDIAN	51.906	0.084	
	MIN, MAX	17.250, 102.868	0.055, 0.112	
	5%, 95%	17.250, 102.868	0.055, 0.112	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0282
	MEAN, GEO MEAN	55.988, 49.589	0.071, 0.071	
	SD, SE	32.3685, 13.2144	0.0078, 0.0045	
	MEDIAN	50.322	0.075	
	MIN, MAX	28.075, 116.308	0.062, 0.076	
	5%, 95%	28.075, 116.308	0.062, 0.076	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	49.089, 42.023	0.056, 0.053	
	SD, SE	29.2167, 13.0661	0.0193, 0.0096	
	MEDIAN	53.238	0.056	
	MIN, MAX	19.754, 92.206	0.036, 0.076	
	5%, 95%	19.754, 92.206	0.036, 0.076	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	5	0.0081
	MEAN, GEO MEAN	52.296, 45.973	0.067, 0.065	
	SD, SE	29.1763, 11.9112	0.0204, 0.0091	
	MEDIAN	51.240	0.072	
	MIN, MAX	21.693, 103.794	0.043, 0.094	
	5%, 95%	21.693, 103.794	0.043, 0.094	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 200 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	3.034, 2.717	
	SD, SE	1.5673, 0.6399	
	MEDIAN	2.510	
	MIN, MAX	1.604, 5.143	
	5%, 95%	1.604, 5.143	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	4.436, 3.758	
	SD, SE	2.6207, 1.0699	
	MEDIAN	4.213	
	MIN, MAX	1.455, 8.410	
	5%, 95%	1.455, 8.410	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	4.559, 3.847	
	SD, SE	2.7668, 1.2374	
	MEDIAN	4.610	
	MIN, MAX	1.336, 8.873	
	5%, 95%	1.336, 8.873	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	3.886, 3.448	
	SD, SE	1.8962, 0.7741	
	MEDIAN	4.010	
	MIN, MAX	1.465, 6.312	
	5%, 95%	1.465, 6.312	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 201 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/mg Creatinine) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6	2	0.0635
	MEAN, GEO MEAN	0.009, 0.007	0.000, NA	
	SD, SE	0.0048, 0.0020	0.0000, 0.0000	
	MEDIAN	0.009	0.000	
	MIN, MAX	0.003, 0.017	0.000, 0.000	
	5%, 95%	0.003, 0.017	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0243
	MEAN, GEO MEAN	0.009, 0.008	0.000, NA	
	SD, SE	0.0052, 0.0021	0.0000, 0.0000	
	MEDIAN	0.008	0.000	
	MIN, MAX	0.005, 0.019	0.000, 0.000	
	5%, 95%	0.005, 0.019	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0146
	MEAN, GEO MEAN	0.008, 0.007	0.000, NA	
	SD, SE	0.0048, 0.0021	0.0000, 0.0000	
	MEDIAN	0.009	0.000	
	MIN, MAX	0.003, 0.015	0.000, 0.000	
	5%, 95%	0.003, 0.015	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0	
Overall*	N	6	5	0.0055
	MEAN, GEO MEAN	0.009, 0.008	0.000, NA	
	SD, SE	0.0046, 0.0019	0.0000, 0.0000	
	MEDIAN	0.009	0.000	
	MIN, MAX	0.004, 0.017	0.000, 0.000	
	5%, 95%	0.004, 0.017	0.000, 0.000	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 202 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.000, NA		
	SD, SE	0.0005, 0.0002		
	MEDIAN	0.000		
	MIN, MAX	0.000, 0.001		
	5%, 95%	0.000, 0.001		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0005, 0.0002		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.001		
	5%, 95%	0.000, 0.001		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0004, 0.0002		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.001		
	5%, 95%	0.000, 0.001		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	0.001, NA		
	SD, SE	0.0005, 0.0002		
	MEDIAN	0.001		
	MIN, MAX	0.000, 0.001		
	5%, 95%	0.000, 0.001		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 203 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	68080.876, 61601.687	79.565, 70.830	
	SD, SE	26039.2173, 10630.4660	51.2575, 36.2445	
	MEDIAN	79107.641	79.565	
	MIN, MAX	20949.848, 87412.052	43.320, 115.809	
	5%, 95%	20949.848, 87412.052	43.320, 115.809	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0282
	MEAN, GEO MEAN	69068.865, 62930.735	94.730, 93.700	
	SD, SE	29783.4963, 12159.0614	16.4762, 9.5126	
	MEDIAN	72661.694	103.788	
	MIN, MAX	26881.034, 114295.450	75.712, 104.690	
	5%, 95%	26881.034, 114295.450	75.712, 104.690	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	53596.816, 43011.516	72.417, 69.294	
	SD, SE	32272.5376, 14432.7176	24.6747, 12.3373	
	MEDIAN	55742.835	69.746	
	MIN, MAX	11067.738, 95783.485	45.486, 104.690	
	5%, 95%	11067.738, 95783.485	45.486, 104.690	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	5	0.0081
	MEAN, GEO MEAN	65164.772, 58044.148	81.764, 78.871	
	SD, SE	28150.9472, 11492.5761	24.3456, 10.8877	
	MEDIAN	71977.959	74.511	
	MIN, MAX	19632.873, 99062.755	54.839, 109.799	
	5%, 95%	19632.873, 99062.755	54.839, 109.799	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/24hr)/cigarette per day)		Analytical Lab: [NBIFO]	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	3969.881, 3749.268	
	SD, SE	1552.3722, 633.7533	
	MEDIAN	3646.083	
	MIN, MAX	2318.472, 6808.809	
	5%, 95%	2318.472, 6808.809	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	
	MEAN, GEO MEAN	5695.530, 4768.962	
	SD, SE	4031.7410, 1645.9514	
	MEDIAN	4776.254	
	MIN, MAX	2408.502, 13290.548	
	5%, 95%	2408.502, 13290.548	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	
	MEAN, GEO MEAN	4742.508, 3937.563	
	SD, SE	3073.5371, 1374.5276	
	MEDIAN	4789.174	
	MIN, MAX	1844.623, 9290.473	
	5%, 95%	1844.623, 9290.473	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	
	MEAN, GEO MEAN	4751.341, 4324.711	
	SD, SE	2249.8673, 918.5045	
	MEDIAN	4386.134	
	MIN, MAX	2480.448, 8299.831	
	5%, 95%	2480.448, 8299.831	
			NA

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	11.045, 9.994	0.013, 0.012	
	SD, SE	4.2243, 1.7246	0.0085, 0.0060	
	MEDIAN	12.834	0.013	
	MIN, MAX	3.399, 14.181	0.007, 0.019	
	5%, 95%	3.399, 14.181	0.007, 0.019	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0275
	MEAN, GEO MEAN	11.205, 10.209	0.015, 0.015	
	SD, SE	4.8317, 1.9725	0.0029, 0.0017	
	MEDIAN	11.788	0.017	
	MIN, MAX	4.361, 18.542	0.012, 0.017	
	5%, 95%	4.361, 18.542	0.012, 0.017	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0200
	MEAN, GEO MEAN	8.695, 6.978	0.012, 0.011	
	SD, SE	5.2354, 2.3413	0.0041, 0.0021	
	MEDIAN	9.043	0.012	
	MIN, MAX	1.796, 15.539	0.007, 0.017	
	5%, 95%	1.796, 15.539	0.007, 0.017	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	5	0.0081
	MEAN, GEO MEAN	10.572, 9.417	0.013, 0.013	
	SD, SE	4.5670, 1.8645	0.0039, 0.0017	
	MEDIAN	11.677	0.012	
	MIN, MAX	3.185, 16.071	0.009, 0.018	
	5%, 95%	3.185, 16.071	0.009, 0.018	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.644, 0.608		
	SD, SE	0.2520, 0.1029		
	MEDIAN	0.592		
	MIN, MAX	0.376, 1.105		
	5%, 95%	0.376, 1.105		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.924, 0.774		
	SD, SE	0.6539, 0.2670		
	MEDIAN	0.775		
	MIN, MAX	0.391, 2.156		
	5%, 95%	0.391, 2.156		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.769, 0.639		
	SD, SE	0.4985, 0.2229		
	MEDIAN	0.777		
	MIN, MAX	0.299, 1.507		
	5%, 95%	0.299, 1.507		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	6		NA
	MEAN, GEO MEAN	0.771, 0.702		
	SD, SE	0.3647, 0.1489		
	MEDIAN	0.712		
	MIN, MAX	0.403, 1.346		
	5%, 95%	0.403, 1.346		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/L)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0651
	MEAN, GEO MEAN	42916.1, 36598.8	36.1, 36.1	
	SD, SE	27913.02, 11395.44	0.00, 0.00	
	MEDIAN	31923.4	36.1	
	MIN, MAX	15404.3, 93914.6	36.1, 36.1	
	5%, 95%	15404.3, 93914.6	36.1, 36.1	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0275
	MEAN, GEO MEAN	43564.7, 37349.6	48.3, 45.6	
	SD, SE	25097.21, 10245.89	21.19, 12.23	
	MEDIAN	36979.7	36.1	
	MIN, MAX	14851.4, 74519.1	36.1, 72.8	
	5%, 95%	14851.4, 74519.1	36.1, 72.8	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0151
	MEAN, GEO MEAN	28148.3, 24212.6	36.1, 36.1	
	SD, SE	14484.66, 6477.74	0.00, 0.00	
	MEDIAN	25926.9	36.1	
	MIN, MAX	8020.1, 44901.7	36.1, 36.1	
	5%, 95%	8020.1, 44901.7	36.1, 36.1	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	5	0.0067
	MEAN, GEO MEAN	40224.0, 34606.9	38.5, 38.3	
	SD, SE	22647.85, 9245.95	5.46, 2.44	
	MEDIAN	33374.7	36.1	
	MIN, MAX	12758.6, 70848.7	36.1, 48.3	
	5%, 95%	12758.6, 70848.7	36.1, 48.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 208 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	2835.8, 2227.5		
	SD, SE	2513.94, 1026.31		
	MEDIAN	2086.4		
	MIN, MAX	946.3, 7826.2		
	5%, 95%	946.3, 7826.2		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	3525.9, 2830.4		
	SD, SE	2429.59, 991.88		
	MEDIAN	2784.8		
	MIN, MAX	1216.4, 6702.7		
	5%, 95%	1216.4, 6702.7		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	2524.2, 2216.6		
	SD, SE	1416.68, 633.56		
	MEDIAN	1954.8		
	MIN, MAX	1266.5, 4321.2		
	5%, 95%	1266.5, 4321.2		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	6		NA
	MEAN, GEO MEAN	2990.8, 2617.2		
	SD, SE	1768.98, 722.18		
	MEDIAN	2419.9		
	MIN, MAX	1431.7, 6090.2		
	5%, 95%	1431.7, 6090.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 209 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/L) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	2	0.0651
	MEAN, GEO MEAN	7.0, 5.9	0.0, NA	
	SD, SE	4.51, 1.84	0.00, 0.00	
	MEDIAN	5.2	0.0	
	MIN, MAX	2.5, 15.2	0.0, 0.0	
	5%, 95%	2.5, 15.2	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	3	0.0250
	MEAN, GEO MEAN	7.1, 6.0	0.0, NA	
	SD, SE	4.09, 1.67	0.00, 0.00	
	MEDIAN	6.0	0.0	
	MIN, MAX	2.4, 12.1	0.0, 0.0	
	5%, 95%	2.4, 12.1	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	4	0.0151
	MEAN, GEO MEAN	4.6, 3.9	0.0, NA	
	SD, SE	2.35, 1.05	0.00, 0.00	
	MEDIAN	4.2	0.0	
	MIN, MAX	1.3, 7.3	0.0, 0.0	
	5%, 95%	1.3, 7.3	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	5	0.0055
	MEAN, GEO MEAN	6.5, 5.6	0.0, NA	
	SD, SE	3.68, 1.50	0.00, 0.00	
	MEDIAN	5.4	0.0	
	MIN, MAX	2.1, 11.5	0.0, 0.0	
	5%, 95%	2.1, 11.5	0.0, 0.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 210 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.5, 0.4		
	SD, SE	0.42, 0.17		
	MEDIAN	0.4		
	MIN, MAX	0.2, 1.3		
	5%, 95%	0.2, 1.3		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.6, 0.4		
	SD, SE	0.40, 0.16		
	MEDIAN	0.5		
	MIN, MAX	0.2, 1.1		
	5%, 95%	0.2, 1.1		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.4, 0.3		
	SD, SE	0.23, 0.10		
	MEDIAN	0.3		
	MIN, MAX	0.2, 0.7		
	5%, 95%	0.2, 0.7		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.5, 0.4		
	SD, SE	0.29, 0.12		
	MEDIAN	0.4		
	MIN, MAX	0.2, 1.0		
	5%, 95%	0.2, 1.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 211 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/24hr) Analytical Lab: INBIFO				P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	5	0.0081
	MEAN, GEO MEAN	33201.994, 29446.306	54.413, 41.136	
	SD, SE	16443.9553, 6713.2166	46.9354, 20.9901	
	MEDIAN	32778.032	39.779	
	MIN, MAX	11447.120, 59281.220	14.880, 132.925	
	5%, 95%	11447.120, 59281.220	14.880, 132.925	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0081
	MEAN, GEO MEAN	34737.115, 29644.668	35.146, 29.986	
	SD, SE	23109.7163, 9434.5022	22.0406, 9.8569	
	MEDIAN	28940.034	35.650	
	MIN, MAX	13685.048, 78161.850	12.896, 70.392	
	5%, 95%	13685.048, 78161.850	12.896, 70.392	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	25853.932, 18736.622	27.836, 26.364	
	SD, SE	24683.2568, 11038.6880	9.8852, 4.4208	
	MEDIAN	16042.225	25.594	
	MIN, MAX	5906.262, 68488.280	15.624, 39.680	
	5%, 95%	5906.262, 68488.280	15.624, 39.680	
	# of BLQ/ALQ Values	0/0	5/0	
Overall*	N	6	6	0.0051
	MEAN, GEO MEAN	32056.944, 27264.865	49.377, 38.249	
	SD, SE	20295.1308, 8285.4525	42.9212, 17.5225	
	MEDIAN	25715.951	37.165	
	MIN, MAX	10346.143, 68643.783	14.467, 132.925	
	5%, 95%	10346.143, 68643.783	14.467, 132.925	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 212 of 264)

Biomarker: Total 3-hydroxycotinine (µg/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	5	0.0081
	MEAN, GEO MEAN	6381.423, 5659.580	10.458, 7.907	
	SD, SE	3160.5282, 1290.2802	9.0208, 4.0342	
	MEDIAN	6299.938	7.646	
	MIN, MAX	2200.136, 11393.850	2.860, 25.548	
	5%, 95%	2200.136, 11393.850	2.860, 25.548	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0081
	MEAN, GEO MEAN	6680.318, 5697.705	6.755, 5.764	
	SD, SE	4441.6877, 1813.3114	4.2360, 1.8944	
	MEDIAN	5562.275	6.852	
	MIN, MAX	2630.266, 15022.708	2.479, 13.529	
	5%, 95%	2630.266, 15022.708	2.479, 13.529	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	4969.126, 3601.179	5.350, 5.067	
	SD, SE	4744.1216, 2121.6357	1.8999, 0.8496	
	MEDIAN	3083.316	4.919	
	MIN, MAX	1135.184, 13163.447	3.003, 7.626	
	5%, 95%	1135.184, 13163.447	3.003, 7.626	
	# of BLQ/ALQ Values	0/0	5/0	
Overall ^b	N	6	6	0.0051
	MEAN, GEO MEAN	6161.345, 5240.307	9.490, 7.352	
	SD, SE	3900.7240, 1592.4639	8.2493, 3.3678	
	MEDIAN	4942.606	7.144	
	MIN, MAX	1988.529, 13193.335	2.781, 25.548	
	5%, 95%	1988.529, 13193.335	2.781, 25.548	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 213 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	1886.926, 1792.193	
	SD, SE	639.6634, 261.1415	
	MEDIAN	1852.551	
	MIN, MAX	954.045, 2964.061	
	5%, 95%	954.045, 2964.061	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	2638.142, 2246.506	
	SD, SE	1731.2715, 706.7886	
	MEDIAN	1879.397	
	MIN, MAX	1222.808, 5570.650	
	5%, 95%	1222.808, 5570.650	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	1981.395, 1715.276	
	SD, SE	1106.5131, 494.8477	
	MEDIAN	2001.295	
	MIN, MAX	823.186, 3424.414	
	5%, 95%	823.186, 3424.414	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	2162.396, 2023.888	
	SD, SE	879.8664, 359.2039	
	MEDIAN	1871.419	
	MIN, MAX	1312.972, 3432.189	
	5%, 95%	1312.972, 3432.189	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 214 of 264)

Biomarker: Total 3-hydroxycotinine ((µg/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	362.667, 344.459		
	SD, SE	122.9436, 50.1915		
	MEDIAN	356.061		
	MIN, MAX	183.367, 569.693		
	5%, 95%	183.367, 569.693		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	507.051, 431.779		
	SD, SE	332.7503, 135.8447		
	MEDIAN	361.220		
	MIN, MAX	235.024, 1070.679		
	5%, 95%	235.024, 1070.679		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	380.824, 329.676		
	SD, SE	212.6719, 95.1097		
	MEDIAN	384.649		
	MIN, MAX	158.216, 658.172		
	5%, 95%	158.216, 658.172		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	415.613, 388.991		
	SD, SE	169.1105, 69.0391		
	MEDIAN	359.687		
	MIN, MAX	252.353, 659.667		
	5%, 95%	252.353, 659.667		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 215 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	5	0.0080
	MEAN, GEO MEAN	26.386, 21.334	0.040, 0.032	
	SD, SE	21.9570, 8.9639	0.0326, 0.0146	
	MEDIAN	20.188	0.025	
	MIN, MAX	9.426, 70.006	0.019, 0.096	
	5%, 95%	9.426, 70.006	0.019, 0.096	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0075
	MEAN, GEO MEAN	28.860, 23.360	0.021, 0.020	
	SD, SE	25.1708, 10.2759	0.0073, 0.0032	
	MEDIAN	19.587	0.026	
	MIN, MAX	14.293, 79.538	0.011, 0.026	
	5%, 95%	14.293, 79.538	0.011, 0.026	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	24.228, 18.306	0.021, 0.020	
	SD, SE	23.6263, 10.5660	0.0070, 0.0031	
	MEDIAN	15.321	0.023	
	MIN, MAX	9.955, 65.930	0.012, 0.028	
	5%, 95%	9.955, 65.930	0.012, 0.028	
	# of BLQ/ALQ Values	0/0	5/0	
Overall ^b	N	6	6	0.0051
	MEAN, GEO MEAN	26.496, 21.465	0.035, 0.028	
	SD, SE	22.6461, 9.2452	0.0306, 0.0125	
	MEDIAN	18.599	0.024	
	MIN, MAX	11.420, 71.825	0.014, 0.096	
	5%, 95%	11.420, 71.825	0.014, 0.096	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 216 of 264)

Biomarker: Total 3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	5	0.0080
	MEAN, GEO MEAN	5.071, 4.100	0.008, 0.006	
	SD, SE	4.2201, 1.7228	0.0059, 0.0027	
	MEDIAN	3.880	0.005	
	MIN, MAX	1.812, 13.455	0.004, 0.018	
	5%, 95%	1.812, 13.455	0.004, 0.018	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0075
	MEAN, GEO MEAN	5.547, 4.490	0.004, 0.004	
	SD, SE	4.8377, 1.9750	0.0014, 0.0006	
	MEDIAN	3.765	0.005	
	MIN, MAX	2.747, 15.287	0.002, 0.005	
	5%, 95%	2.747, 15.287	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0119
	MEAN, GEO MEAN	4.657, 3.518	0.004, 0.004	
	SD, SE	4.5411, 2.0309	0.0013, 0.0006	
	MEDIAN	2.945	0.004	
	MIN, MAX	1.913, 12.672	0.002, 0.005	
	5%, 95%	1.913, 12.672	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	5/0	
Overall ^b	N	6	6	0.0051
	MEAN, GEO MEAN	5.093, 4.126	0.007, 0.005	
	SD, SE	4.3527, 1.7770	0.0056, 0.0023	
	MEDIAN	3.575	0.005	
	MIN, MAX	2.195, 13.805	0.003, 0.018	
	5%, 95%	2.195, 13.805	0.003, 0.018	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 217 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	1.505, 1.298		
	SD, SE	1.0220, 0.4172		
	MEDIAN	1.142		
	MIN, MAX	0.680, 3.500		
	5%, 95%	0.680, 3.500		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	2.096, 1.770		
	SD, SE	1.3236, 0.5404		
	MEDIAN	1.534		
	MIN, MAX	0.739, 3.977		
	5%, 95%	0.739, 3.977		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1.955, 1.676		
	SD, SE	1.0343, 0.4626		
	MEDIAN	1.757		
	MIN, MAX	0.553, 3.297		
	5%, 95%	0.553, 3.297		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	1.807, 1.601		
	SD, SE	1.0054, 0.4104		
	MEDIAN	1.548		
	MIN, MAX	0.763, 3.591		
	5%, 95%	0.763, 3.591		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 218 of 264)

Biomarker: Total 3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	0.290, 0.250	
	SD, SE	0.1964, 0.0802	
	MEDIAN	0.220	
	MIN, MAX	0.131, 0.673	
	5%, 95%	0.131, 0.673	
Week 2	# of BLQ/ALQ Values	0/0	
	N	6	NA
	MEAN, GEO MEAN	0.403, 0.340	
	SD, SE	0.2544, 0.1038	
	MEDIAN	0.295	
	MIN, MAX	0.142, 0.764	
Week 3	5%, 95%	0.142, 0.764	
	# of BLQ/ALQ Values	0/0	
	N	5	NA
	MEAN, GEO MEAN	0.376, 0.322	
	SD, SE	0.1990, 0.0890	
	MEDIAN	0.338	
Overall*	MIN, MAX	0.106, 0.634	
	5%, 95%	0.106, 0.634	
	# of BLQ/ALQ Values	0/0	
	N	6	NA
	MEAN, GEO MEAN	0.347, 0.308	
	SD, SE	0.1931, 0.0788	
	MEDIAN	0.298	
	MIN, MAX	0.147, 0.690	
	5%, 95%	0.147, 0.690	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	5	0.0075
	MEAN, GEO MEAN	18760.8, 17494.6	24.5, 20.3	
	SD, SE	6817.90, 2783.39	16.64, 7.44	
	MEDIAN	20361.6	12.4	
	MIN, MAX	8417.0, 25578.5	12.4, 44.5	
	5%, 95%	8417.0, 25578.5	12.4, 44.5	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0067
	MEAN, GEO MEAN	19977.0, 17594.2	18.3, 15.8	
	SD, SE	10727.64, 4379.54	13.19, 5.90	
	MEDIAN	18523.4	12.4	
	MIN, MAX	7560.8, 37689.3	12.4, 41.9	
	5%, 95%	7560.8, 37689.3	12.4, 41.9	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0075
	MEAN, GEO MEAN	12925.5, 10547.5	12.4, 12.4	
	SD, SE	9343.85, 4178.70	0.00, 0.00	
	MEDIAN	9437.8	12.4	
	MIN, MAX	4279.9, 27954.4	12.4, 12.4	
	5%, 95%	4279.9, 27954.4	12.4, 12.4	
	# of BLQ/ALQ Values	0/0	5/0	
Overall ^b	N	6	6	0.0043
	MEAN, GEO MEAN	18260.5, 16211.6	20.6, 17.8	
	SD, SE	9101.47, 3715.66	12.90, 5.27	
	MEDIAN	17343.5	12.4	
	MIN, MAX	6752.6, 31633.9	12.4, 40.9	
	5%, 95%	6752.6, 31633.9	12.4, 40.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 220 of 264)

Biomarker: Total 3-hydroxycotinine (ng/mL)		Analytical Lab: INRIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6	5	0.0075
	MEAN, GEO MEAN	3605.8, 3362.4	4.7, 3.9	
	SD, SE	1310.43, 534.98	3.21, 1.44	
	MEDIAN	3913.5	2.4	
	MIN, MAX	1617.7, 4916.2	2.4, 8.6	
	5%, 95%	1617.7, 4916.2	2.4, 8.6	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0067
	MEAN, GEO MEAN	3839.6, 3381.6	3.5, 3.1	
	SD, SE	2061.85, 841.75	2.55, 1.14	
	MEDIAN	3560.2	2.4	
	MIN, MAX	1453.2, 7243.9	2.4, 8.1	
	5%, 95%	1453.2, 7243.9	2.4, 8.1	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	5	0.0075
	MEAN, GEO MEAN	2484.3, 2027.2	2.4, 2.4	
	SD, SE	1795.88, 803.14	0.00, 0.00	
	MEDIAN	1813.9	2.4	
	MIN, MAX	822.6, 5372.8	2.4, 2.4	
	5%, 95%	822.6, 5372.8	2.4, 2.4	
	# of BLQ/ALQ Values	0/0	5/0	
Overall*	N	6	6	0.0043
	MEAN, GEO MEAN	3509.7, 3115.9	4.0, 3.4	
	SD, SE	1749.33, 714.16	2.50, 1.02	
	MEDIAN	3333.4	2.4	
	MIN, MAX	1297.8, 6080.1	2.4, 7.9	
	5%, 95%	1297.8, 6080.1	2.4, 7.9	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: INB/FO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	1189.4, 1064.8		
	SD, SE	551.72, 225.24		
	MEDIAN	1119.4		
	MIN, MAX	389.4, 2083.0		
	5%, 95%	389.4, 2083.0		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1510.8, 1333.3		
	SD, SE	765.95, 312.70		
	MEDIAN	1572.6		
	MIN, MAX	617.6, 2591.0		
	5%, 95%	617.6, 2591.0		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1034.0, 965.6		
	SD, SE	388.91, 173.93		
	MEDIAN	1243.6		
	MIN, MAX	524.3, 1397.7		
	5%, 95%	524.3, 1397.7		
	# of BLQ/ALQ Values	0/0		
Overall†	N	6		NA
	MEAN, GEO MEAN	1270.5, 1221.9		
	SD, SE	371.77, 151.78		
	MEDIAN	1317.4		
	MIN, MAX	756.2, 1776.3		
	5%, 95%	756.2, 1776.3		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

† Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	228.6, 204.6		
	SD, SE	106.07, 43.30		
	MEDIAN	215.2		
	MIN, MAX	74.8, 400.4		
	5%, 95%	74.8, 400.4		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	290.4, 256.3		
	SD, SE	147.23, 60.10		
	MEDIAN	302.3		
	MIN, MAX	118.7, 498.0		
	5%, 95%	118.7, 498.0		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	198.7, 185.6		
	SD, SE	74.73, 33.42		
	MEDIAN	239.0		
	MIN, MAX	100.8, 268.6		
	5%, 95%	100.8, 268.6		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	6		NA
	MEAN, GEO MEAN	244.2, 234.9		
	SD, SE	71.44, 29.17		
	MEDIAN	253.2		
	MIN, MAX	145.4, 341.4		
	5%, 95%	145.4, 341.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	6	0.0051
	MEAN, GEO MEAN	21538.800, 17732.715	22.473, 20.850	
	SD, SE	11226.8961, 4583.3611	9.6010, 3.9196	
	MEDIAN	21849.563	19.360	
	MIN, MAX	3897.624, 34631.742	13.200, 35.288	
	5%, 95%	3897.624, 34631.742	13.200, 35.288	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	21942.772, 19820.873	25.654, 23.904	
	SD, SE	8654.5985, 3533.2251	9.4756, 3.5815	
	MEDIAN	25091.510	30.250	
	MIN, MAX	6895.195, 28995.975	11.440, 37.400	
	5%, 95%	6895.195, 28995.975	11.440, 37.400	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	18359.870, 13658.400	22.446, 21.506	
	SD, SE	11454.7088, 5122.7015	7.1197, 2.6910	
	MEDIAN	20410.460	20.680	
	MIN, MAX	2437.770, 31425.320	13.860, 32.010	
	5%, 95%	2437.770, 31425.320	13.860, 32.010	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	20878.245, 17708.653	23.599, 22.442	
	SD, SE	9961.1819, 4066.6355	7.6547, 2.7064	
	MEDIAN	22902.038	23.467	
	MIN, MAX	4410.196, 31587.791	12.833, 33.457	
	5%, 95%	4410.196, 31587.791	12.833, 33.457	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (µg/24hr) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	6	0.0051
	MEAN, GEO MEAN	3795.136, 3124.504	3.960, 3.674	
	SD, SE	1978.1792, 807.5883	1.6917, 0.6906	
	MEDIAN	3849.893	3.412	
	MIN, MAX	686.761, 6102.113	2.326, 6.218	
	5%, 95%	686.761, 6102.113	2.326, 6.218	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	3866.317, 3492.438	4.520, 4.212	
	SD, SE	1524.9404, 622.5543	1.6696, 0.6310	
	MEDIAN	4421.124	5.330	
	MIN, MAX	1214.933, 5109.091	2.016, 6.590	
	5%, 95%	1214.933, 5109.091	2.016, 6.590	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	3235.009, 2406.610	3.955, 3.789	
	SD, SE	2018.3196, 902.6199	1.2545, 0.4742	
	MEDIAN	3596.323	3.644	
	MIN, MAX	429.535, 5537.141	2.442, 5.640	
	5%, 95%	429.535, 5537.141	2.442, 5.640	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	3678.747, 3120.264	4.158, 3.954	
	SD, SE	1755.1605, 716.5413	1.3489, 0.4769	
	MEDIAN	4035.339	4.135	
	MIN, MAX	777.076, 5565.769	2.261, 5.895	
	5%, 95%	777.076, 5565.769	2.261, 5.895	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	1229.881, 1079.267		
	SD, SE	823.2641, 336.0961		
	MEDIAN	982.101		
	MIN, MAX	649.604, 2885.979		
	5%, 95%	649.604, 2885.979		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1914.135, 1502.048		
	SD, SE	1583.3261, 646.3902		
	MEDIAN	1254.576		
	MIN, MAX	689.520, 4832.663		
	5%, 95%	689.520, 4832.663		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1797.060, 1250.382		
	SD, SE	1634.6604, 731.0423		
	MEDIAN	1020.523		
	MIN, MAX	406.295, 4282.406		
	5%, 95%	406.295, 4282.406		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	1607.238, 1310.722		
	SD, SE	1140.8004, 465.7298		
	MEDIAN	1107.553		
	MIN, MAX	581.806, 3359.319		
	5%, 95%	581.806, 3359.319		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((µg/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	216.705, 190.167	
	SD, SE	145.0589, 59.2201	
	MEDIAN	173.047	
	MIN, MAX	114.460, 508.509	
	5%, 95%	114.460, 508.509	
Week 2	# of BLQ/ALQ Values	0/0	
	N	6	NA
	MEAN, GEO MEAN	337.270, 264.661	
	SD, SE	278.9821, 113.8939	
	MEDIAN	221.056	
	MIN, MAX	121.493, 851.515	
Week 3	5%, 95%	121.493, 851.515	
	# of BLQ/ALQ Values	0/0	
	N	5	NA
	MEAN, GEO MEAN	316.642, 220.317	
	SD, SE	288.0272, 128.8097	
	MEDIAN	179.816	
Overall*	MIN, MAX	71.589, 754.560	
	5%, 95%	71.589, 754.560	
	# of BLQ/ALQ Values	0/0	
	N	6	NA
	MEAN, GEO MEAN	283.195, 230.949	
	SD, SE	201.0090, 82.0616	
Overall*	MEDIAN	195.151	
	MIN, MAX	102.514, 591.912	
	5%, 95%	102.514, 591.912	
	# of BLQ/ALQ Values	0/0	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/mg Creatinine) Analytical Lab: INBIFO				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	6	0.0050
	MEAN, GEO MEAN	15.933, 12.847	0.016, 0.014	
	SD, SE	9.1696, 3.7435	0.0098, 0.0040	
	MEDIAN	17.813	0.015	
	MIN, MAX	3.209, 24.408	0.006, 0.034	
	5%, 95%	3.209, 24.408	0.006, 0.034	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	17.374, 15.619	0.018, 0.016	
	SD, SE	8.1799, 3.3394	0.0107, 0.0041	
	MEDIAN	16.762	0.014	
	MIN, MAX	7.201, 27.449	0.007, 0.038	
	5%, 95%	7.201, 27.449	0.007, 0.038	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0056
	MEAN, GEO MEAN	16.373, 13.344	0.018, 0.017	
	SD, SE	9.6689, 4.3241	0.0051, 0.0019	
	MEDIAN	19.648	0.021	
	MIN, MAX	4.351, 25.375	0.011, 0.023	
	5%, 95%	4.351, 25.375	0.011, 0.023	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	16.432, 14.120	0.019, 0.018	
	SD, SE	8.4653, 3.4559	0.0077, 0.0027	
	MEDIAN	17.962	0.018	
	MIN, MAX	4.920, 25.193	0.009, 0.030	
	5%, 95%	4.920, 25.193	0.009, 0.030	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (µg/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	6	0.0049
	MEAN, GEO MEAN	2.807, 2.263	0.003, 0.002	
	SD, SE	1.6159, 0.6597	0.0017, 0.0007	
	MEDIAN	3.139	0.003	
	MIN, MAX	0.565, 4.301	0.001, 0.006	
	5%, 95%	0.565, 4.301	0.001, 0.006	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0032
	MEAN, GEO MEAN	3.061, 2.752	0.003, 0.003	
	SD, SE	1.4415, 0.5885	0.0020, 0.0008	
	MEDIAN	2.954	0.002	
	MIN, MAX	1.269, 4.837	0.001, 0.007	
	5%, 95%	1.269, 4.837	0.001, 0.007	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0046
	MEAN, GEO MEAN	2.885, 2.352	0.003, 0.003	
	SD, SE	1.7035, 0.7618	0.0011, 0.0004	
	MEDIAN	3.462	0.004	
	MIN, MAX	0.767, 4.471	0.002, 0.004	
	5%, 95%	0.767, 4.471	0.002, 0.004	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	2.896, 2.488	0.003, 0.003	
	SD, SE	1.4915, 0.6089	0.0017, 0.0006	
	MEDIAN	3.165	0.003	
	MIN, MAX	0.867, 4.439	0.001, 0.006	
	5%, 95%	0.867, 4.439	0.001, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.913, 0.782		
	SD, SE	0.6117, 0.2497		
	MEDIAN	0.626		
	MIN, MAX	0.446, 2.028		
	5%, 95%	0.446, 2.028		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1.462, 1.184		
	SD, SE	1.0294, 0.4203		
	MEDIAN	1.066		
	MIN, MAX	0.510, 3.058		
	5%, 95%	0.510, 3.058		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1.671, 1.222		
	SD, SE	1.4941, 0.6682		
	MEDIAN	0.982		
	MIN, MAX	0.442, 4.090		
	5%, 95%	0.442, 4.090		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	1.293, 1.054		
	SD, SE	0.8934, 0.3647		
	MEDIAN	0.927		
	MIN, MAX	0.466, 2.611		
	5%, 95%	0.466, 2.611		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 230 of 264)

Biomarker: Total Cotinine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.161, 0.138		
	SD, SE	0.1076, 0.0439		
	MEDIAN	0.111		
	MIN, MAX	0.079, 0.357		
	5%, 95%	0.079, 0.357		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.258, 0.209		
	SD, SE	0.1813, 0.0740		
	MEDIAN	0.188		
	MIN, MAX	0.090, 0.539		
	5%, 95%	0.090, 0.539		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.295, 0.215		
	SD, SE	0.2634, 0.1178		
	MEDIAN	0.173		
	MIN, MAX	0.078, 0.721		
	5%, 95%	0.078, 0.721		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	0.228, 0.186		
	SD, SE	0.1573, 0.0642		
	MEDIAN	0.164		
	MIN, MAX	0.082, 0.460		
	5%, 95%	0.082, 0.460		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 231 of 264)

Biomarker: Total Cotinine (nmol/L) Analytical Lab: INBIFO				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	6	0.0028
	MEAN, GEO MEAN	14356.4, 10535.4	11.0, 11.0	
	SD, SE	13129.60, 5360.14	0.00, 0.00	
	MEDIAN	11017.2	11.0	
	MIN, MAX	2865.9, 39806.6	11.0, 11.0	
	5%, 95%	2865.9, 39806.6	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0015
	MEAN, GEO MEAN	14653.4, 11763.7	11.0, 11.0	
	SD, SE	10167.85, 4151.01	0.00, 0.00	
	MEDIAN	11093.9	11.0	
	MIN, MAX	3809.5, 30867.0	11.0, 11.0	
	5%, 95%	3809.5, 30867.0	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	9971.7, 7688.8	11.0, 11.0	
	SD, SE	6819.34, 3049.70	0.00, 0.00	
	MEDIAN	8330.8	11.0	
	MIN, MAX	1766.5, 20274.4	11.0, 11.0	
	5%, 95%	1766.5, 20274.4	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0008
	MEAN, GEO MEAN	13463.2, 10521.5	11.0, 11.0	
	SD, SE	9773.22, 3989.90	0.00, 0.00	
	MEDIAN	10588.5	11.0	
	MIN, MAX	2814.0, 30316.0	11.0, 11.0	
	5%, 95%	2814.0, 30316.0	11.0, 11.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 232 of 264)

Biomarker: Total Cotinine (ng/mL) Analytical Lab: INBIFO				P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	6	0.0028
	MEAN, GEO MEAN	2529.6, 1856.3	1.9, 1.9	
	SD, SE	2313.43, 944.45	0.00, 0.00	
	MEDIAN	1941.2	1.9	
	MIN, MAX	505.0, 7013.9	1.9, 1.9	
	5%, 95%	505.0, 7013.9	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	6/0	
Week 2	N	6	7	0.0015
	MEAN, GEO MEAN	2581.9, 2072.8	1.9, 1.9	
	SD, SE	1791.59, 731.41	0.00, 0.00	
	MEDIAN	1954.8	1.9	
	MIN, MAX	671.2, 5438.8	1.9, 1.9	
	5%, 95%	671.2, 5438.8	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	7/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	1757.0, 1354.8	1.9, 1.9	
	SD, SE	1201.54, 537.34	0.00, 0.00	
	MEDIAN	1467.9	1.9	
	MIN, MAX	311.3, 3572.3	1.9, 1.9	
	5%, 95%	311.3, 3572.3	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	8	0.0008
	MEAN, GEO MEAN	2372.2, 1853.9	1.9, 1.9	
	SD, SE	1722.05, 703.03	0.00, 0.00	
	MEDIAN	1865.7	1.9	
	MIN, MAX	495.8, 5341.7	1.9, 1.9	
	5%, 95%	495.8, 5341.7	1.9, 1.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 233 of 264)

Biomarker: Total Cotinine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	945.0, 641.2		
	SD, SE	1165.85, 475.96		
	MEDIAN	490.7		
	MIN, MAX	356.4, 3317.2		
	5%, 95%	356.4, 3317.2		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1237.2, 891.5		
	SD, SE	1051.58, 429.31		
	MEDIAN	780.9		
	MIN, MAX	381.0, 2806.1		
	5%, 95%	381.0, 2806.1		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	962.2, 703.9		
	SD, SE	810.58, 362.50		
	MEDIAN	418.7		
	MIN, MAX	294.4, 1991.8		
	5%, 95%	294.4, 1991.8		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	1043.2, 790.8		
	SD, SE	884.68, 361.17		
	MEDIAN	661.9		
	MIN, MAX	384.4, 2604.3		
	5%, 95%	384.4, 2604.3		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 234 of 264)

Biomarker: Total Cotinine (ng/mL/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	166.5, 113.0	
	SD, SE	205.43, 83.87	
	MEDIAN	86.5	
	MIN, MAX	62.8, 584.5	
	5%, 95%	62.8, 584.5	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	218.0, 157.1	
	SD, SE	185.29, 75.64	
	MEDIAN	137.6	
	MIN, MAX	67.1, 494.4	
	5%, 95%	67.1, 494.4	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	169.6, 124.1	
	SD, SE	142.83, 63.88	
	MEDIAN	73.8	
	MIN, MAX	51.9, 351.0	
	5%, 95%	51.9, 351.0	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	183.8, 139.4	
	SD, SE	155.89, 63.64	
	MEDIAN	116.7	
	MIN, MAX	67.7, 458.9	
	5%, 95%	67.7, 458.9	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 235 of 264)

Biomarker: Total Nicotine (nmol/24hr)		Analytical Lab: INBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	13340.083, 10943.435	31.361, 28.707	
	SD, SE	8949.6828, 3653.6927	14.0233, 8.0963	
	MEDIAN	10205.028	38.100	
	MIN, MAX	5497.128, 25327.788	15.240, 40.742	
	5%, 95%	5497.128, 25327.788	15.240, 40.742	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0081
	MEAN, GEO MEAN	12368.978, 11224.563	40.565, 40.139	
	SD, SE	5727.7162, 2338.3303	6.8172, 3.0487	
	MEDIAN	11942.637	36.830	
	MIN, MAX	6300.791, 19866.660	34.925, 51.376	
	5%, 95%	6300.791, 19866.660	34.925, 51.376	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	9383.015, 8059.175	29.054, 27.748	
	SD, SE	4868.4540, 2177.2388	9.1357, 3.4530	
	MEDIAN	9143.680	26.213	
	MIN, MAX	2723.706, 14156.770	16.002, 40.640	
	5%, 95%	2723.706, 14156.770	16.002, 40.640	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	6	7	0.0034
	MEAN, GEO MEAN	12229.584, 10705.606	31.847, 31.289	
	SD, SE	6469.9832, 2641.3596	6.2904, 2.3775	
	MEDIAN	11297.326	33.528	
	MIN, MAX	4876.534, 19783.739	22.860, 39.298	
	5%, 95%	4876.534, 19783.739	22.860, 39.298	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 236 of 264)

Biomarker: Total Nicotine (ug/24hr) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	2163.761, 1775.025	5.087, 4.656	
	SD, SE	1451.6384, 592.6289	2.2745, 1.3132	
	MEDIAN	1655.256	6.180	
	MIN, MAX	891.634, 4108.167	2.472, 6.608	
	5%, 95%	891.634, 4108.167	2.472, 6.608	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0081
	MEAN, GEO MEAN	2006.248, 1820.624	6.580, 6.511	
	SD, SE	929.0356, 379.2772	1.1057, 0.4945	
	MEDIAN	1937.096	5.974	
	MIN, MAX	1021.988, 3222.372	5.665, 8.333	
	5%, 95%	1021.988, 3222.372	5.665, 8.333	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0058
	MEAN, GEO MEAN	1521.925, 1307.198	4.713, 4.501	
	SD, SE	789.6633, 353.1482	1.4816, 0.5600	
	MEDIAN	1483.105	4.252	
	MIN, MAX	441.785, 2296.228	2.596, 6.592	
	5%, 95%	441.785, 2296.228	2.596, 6.592	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	7	0.0034
	MEAN, GEO MEAN	1983.638, 1736.449	5.166, 5.075	
	SD, SE	1049.4312, 428.4285	1.0202, 0.3856	
	MEDIAN	1832.426	5.439	
	MIN, MAX	790.974, 3208.922	3.708, 6.374	
	5%, 95%	790.974, 3208.922	3.708, 6.374	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 237 of 264)

Biomarker: Total Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	853.074, 666.051	
	SD, SE	687.2070, 280.5511	
	MEDIAN	667.862	
	MIN, MAX	305.396, 2110.649	
	5%, 95%	305.396, 2110.649	
Week 2	# of BLQ/ALQ Values	0/0	
	N	6	
	MEAN, GEO MEAN	1143.254, 850.610	
	SD, SE	1002.1522, 409.1269	
	MEDIAN	683.182	
	MIN, MAX	341.887, 2887.235	
Week 3	5%, 95%	341.887, 2887.235	
	# of BLQ/ALQ Values	0/0	
	N	5	
	MEAN, GEO MEAN	964.053, 737.791	
	SD, SE	833.1631, 372.6019	
	MEDIAN	507.982	
Overall*	MIN, MAX	344.237, 2334.363	
	5%, 95%	344.237, 2334.363	
	# of BLQ/ALQ Values	0/0	
	N	6	
	MEAN, GEO MEAN	981.707, 808.034	
	SD, SE	652.4491, 266.3612	
Overall*	MEDIAN	772.619	
	MIN, MAX	385.088, 1874.379	
	5%, 95%	385.088, 1874.379	
			NA

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine ((µg/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	138.369, 108.033		
	SD, SE	111.4649, 45.5054		
	MEDIAN	108.328		
	MIN, MAX	49.535, 342.347		
	5%, 95%	49.535, 342.347		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	185.436, 137.969		
	SD, SE	162.5493, 66.3605		
	MEDIAN	110.812		
	MIN, MAX	55.454, 468.310		
	5%, 95%	55.454, 468.310		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	156.369, 119.670		
	SD, SE	135.1391, 60.4361		
	MEDIAN	82.395		
	MIN, MAX	55.835, 378.634		
	5%, 95%	55.835, 378.634		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	159.233, 131.063		
	SD, SE	105.8274, 43.2039		
	MEDIAN	125.319		
	MIN, MAX	62.461, 304.025		
	5%, 95%	62.461, 304.025		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (nmol/mg Creatinine) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	9.381, 7.928	0.024, 0.022	
	SD, SE	5.4803, 2.2373	0.0129, 0.0074	
	MEDIAN	8.947	0.019	
	MIN, MAX	2.896, 17.795	0.015, 0.039	
	5%, 95%	2.896, 17.795	0.015, 0.039	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0081
	MEAN, GEO MEAN	9.755, 8.845	0.031, 0.029	
	SD, SE	4.6862, 1.9131	0.0118, 0.0053	
	MEDIAN	9.474	0.027	
	MIN, MAX	4.131, 17.906	0.016, 0.044	
	5%, 95%	4.131, 17.906	0.016, 0.044	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0057
	MEAN, GEO MEAN	8.488, 7.874	0.021, 0.020	
	SD, SE	3.6972, 1.6534	0.0064, 0.0024	
	MEDIAN	6.628	0.024	
	MIN, MAX	4.861, 13.377	0.013, 0.029	
	5%, 95%	4.861, 13.377	0.013, 0.029	
	# of BLQ/ALQ Values	0/0	7/0	
Overall*	N	6	7	0.0034
	MEAN, GEO MEAN	9.367, 8.525	0.025, 0.024	
	SD, SE	4.2474, 1.7340	0.0072, 0.0027	
	MEDIAN	9.697	0.025	
	MIN, MAX	4.390, 15.711	0.015, 0.034	
	5%, 95%	4.390, 15.711	0.015, 0.034	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 240 of 264)

Biomarker: Total Nicotine (ug/mg Creatinine)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0282
	MEAN, GEO MEAN	1.522, 1.286	0.004, 0.003	
	SD, SE	0.8887, 0.3628	0.0021, 0.0012	
	MEDIAN	1.451	0.003	
	MIN, MAX	0.470, 2.886	0.002, 0.006	
	5%, 95%	0.470, 2.886	0.002, 0.006	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0078
	MEAN, GEO MEAN	1.582, 1.434	0.005, 0.005	
	SD, SE	0.7601, 0.3103	0.0019, 0.0008	
	MEDIAN	1.537	0.004	
	MIN, MAX	0.670, 2.904	0.003, 0.007	
	5%, 95%	0.670, 2.904	0.003, 0.007	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0053
	MEAN, GEO MEAN	1.377, 1.277	0.003, 0.003	
	SD, SE	0.5999, 0.2683	0.0011, 0.0004	
	MEDIAN	1.075	0.004	
	MIN, MAX	0.788, 2.170	0.002, 0.005	
	5%, 95%	0.788, 2.170	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	7	0.0032
	MEAN, GEO MEAN	1.519, 1.383	0.004, 0.004	
	SD, SE	0.6888, 0.2812	0.0013, 0.0005	
	MEDIAN	1.573	0.004	
	MIN, MAX	0.712, 2.548	0.002, 0.006	
	5%, 95%	0.712, 2.548	0.002, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 241 of 264)

Biomarker: Total Nicotine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.615, 0.483		
	SD, SE	0.4755, 0.1941		
	MEDIAN	0.496		
	MIN, MAX	0.161, 1.483		
	5%, 95%	0.161, 1.483		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.878, 0.670		
	SD, SE	0.6766, 0.2762		
	MEDIAN	0.570		
	MIN, MAX	0.207, 1.827		
	5%, 95%	0.207, 1.827		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.933, 0.721		
	SD, SE	0.7763, 0.3472		
	MEDIAN	0.810		
	MIN, MAX	0.331, 2.230		
	5%, 95%	0.331, 2.230		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.786, 0.648		
	SD, SE	0.5055, 0.2064		
	MEDIAN	0.636		
	MIN, MAX	0.236, 1.448		
	5%, 95%	0.236, 1.448		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 242 of 264)

Biomarker: Total Nicotine (($\mu\text{g}/\text{mg}$ Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.100, 0.078		
	SD, SE	0.0774, 0.0316		
	MEDIAN	0.081		
	MIN, MAX	0.026, 0.241		
	5%, 95%	0.026, 0.241		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.143, 0.109		
	SD, SE	0.1095, 0.0447		
	MEDIAN	0.093		
	MIN, MAX	0.034, 0.296		
	5%, 95%	0.034, 0.296		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.151, 0.117		
	SD, SE	0.1261, 0.0564		
	MEDIAN	0.131		
	MIN, MAX	0.054, 0.362		
	5%, 95%	0.054, 0.362		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	0.128, 0.105		
	SD, SE	0.0822, 0.0335		
	MEDIAN	0.103		
	MIN, MAX	0.038, 0.235		
	5%, 95%	0.038, 0.235		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (nmol/L) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0256
	MEAN, GEO MEAN	9798.9, 6501.7	12.7, 12.7	
	SD, SE	10412.65, 4250.94	0.00, 0.00	
	MEDIAN	4765.0	12.7	
	MIN, MAX	2468.7, 29112.4	12.7, 12.7	
	5%, 95%	2468.7, 29112.4	12.7, 12.7	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0067
	MEAN, GEO MEAN	8934.2, 6661.8	20.0, 16.7	
	SD, SE	7476.72, 3052.36	16.41, 7.34	
	MEDIAN	5769.3	12.7	
	MIN, MAX	2954.7, 21362.0	12.7, 49.4	
	5%, 95%	2954.7, 21362.0	12.7, 49.4	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	5251.1, 4536.8	12.7, 12.7	
	SD, SE	2902.43, 1298.01	0.00, 0.00	
	MEDIAN	5824.0	12.7	
	MIN, MAX	1973.7, 9133.4	12.7, 12.7	
	5%, 95%	1973.7, 9133.4	12.7, 12.7	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	7	0.0021
	MEAN, GEO MEAN	8500.5, 6413.7	14.4, 14.0	
	SD, SE	7026.29, 2868.47	4.61, 1.74	
	MEDIAN	5421.7	12.7	
	MIN, MAX	2744.5, 19869.3	12.7, 24.9	
	5%, 95%	2744.5, 19869.3	12.7, 24.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 244 of 264)

Biomarker: Total Nicotine (ng/mL) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	3	0.0256
	MEAN, GEO MEAN	1589.4, 1054.6	2.1, 2.1	
	SD, SE	1688.92, 689.50	0.00, 0.00	
	MEDIAN	772.9	2.1	
	MIN, MAX	400.4, 4722.0	2.1, 2.1	
	5%, 95%	400.4, 4722.0	2.1, 2.1	
	# of BLQ/ALQ Values	0/0	3/0	
Week 2	N	6	5	0.0067
	MEAN, GEO MEAN	1449.1, 1080.5	3.3, 2.7	
	SD, SE	1212.72, 495.09	2.64, 1.18	
	MEDIAN	935.8	2.1	
	MIN, MAX	479.3, 3464.9	2.1, 8.0	
	5%, 95%	479.3, 3464.9	2.1, 8.0	
	# of BLQ/ALQ Values	0/0	4/0	
Week 3	N	5	7	0.0021
	MEAN, GEO MEAN	851.7, 735.9	2.1, 2.1	
	SD, SE	470.78, 210.54	0.00, 0.00	
	MEDIAN	944.7	2.1	
	MIN, MAX	320.1, 1481.4	2.1, 2.1	
	5%, 95%	320.1, 1481.4	2.1, 2.1	
	# of BLQ/ALQ Values	0/0	7/0	
Overall ^b	N	6	7	0.0021
	MEAN, GEO MEAN	1378.8, 1040.3	2.4, 2.3	
	SD, SE	1139.66, 465.26	0.76, 0.29	
	MEDIAN	879.4	2.1	
	MIN, MAX	445.2, 3222.8	2.1, 4.1	
	5%, 95%	445.2, 3222.8	2.1, 4.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 245 of 264)

Biomarker: Total Nicotine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	701.4, 395.7		
	SD, SE	880.12, 359.31		
	MEDIAN	404.2		
	MIN, MAX	123.4, 2426.0		
	5%, 95%	123.4, 2426.0		
Week 2	# of BLQ/ALQ Values	0/0		NA
	N	6		
	MEAN, GEO MEAN	778.0, 504.8		
	SD, SE	724.77, 295.89		
	MEDIAN	531.5		
	MIN, MAX	147.7, 1942.0		
Week 3	5%, 95%	147.7, 1942.0		NA
	# of BLQ/ALQ Values	0/0		
	N	5		
	MEAN, GEO MEAN	528.0, 415.4		
	SD, SE	386.33, 172.77		
	MEDIAN	329.0		
Overall ^b	MIN, MAX	140.5, 1085.8		NA
	5%, 95%	140.5, 1085.8		
	# of BLQ/ALQ Values	0/0		
	N	6		
	MEAN, GEO MEAN	677.1, 490.8		
	SD, SE	573.72, 234.22		
	MEDIAN	562.7		
	MIN, MAX	137.2, 1709.7		
	5%, 95%	137.2, 1709.7		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 246 of 264)

Biomarker: Total Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	113.8, 64.2	
	SD, SE	142.76, 58.28	
	MEDIAN	65.6	
	MIN, MAX	20.0, 393.5	
	5%, 95%	20.0, 393.5	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	126.2, 81.9	
	SD, SE	117.55, 47.99	
	MEDIAN	86.2	
	MIN, MAX	24.0, 315.0	
	5%, 95%	24.0, 315.0	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	85.7, 67.4	
	SD, SE	62.66, 28.02	
	MEDIAN	53.4	
	MIN, MAX	22.8, 176.1	
	5%, 95%	22.8, 176.1	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	109.9, 79.7	
	SD, SE	93.03, 37.98	
	MEDIAN	91.3	
	MIN, MAX	22.3, 277.3	
	5%, 95%	22.3, 277.3	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 247 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	8	0.0024
	MEAN, GEO MEAN	27286.763, 24423.243	27.743, 20.815	
	SD, SE	13018.2385, 5314.6736	19.8790, 7.0283	
	MEDIAN	26551.035	23.760	
	MIN, MAX	9903.928, 47408.910	5.880, 56.550	
	5%, 95%	9903.928, 47408.910	5.880, 56.550	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	28780.750, 23570.930	26.811, 22.854	
	SD, SE	20864.6837, 8517.9715	15.6177, 5.9029	
	MEDIAN	24714.348	23.120	
	MIN, MAX	9062.489, 67799.170	10.712, 47.850	
	5%, 95%	9062.489, 67799.170	10.712, 47.850	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	20684.366, 15880.862	22.055, 19.578	
	SD, SE	17932.5493, 8019.6799	11.5204, 5.1521	
	MEDIAN	13910.514	18.228	
	MIN, MAX	5533.662, 51582.300	9.450, 36.375	
	5%, 95%	5533.662, 51582.300	9.450, 36.375	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	26279.497, 22293.290	23.547, 19.730	
	SD, SE	16487.3011, 6730.9125	13.4248, 4.7464	
	MEDIAN	21636.072	24.725	
	MIN, MAX	8166.693, 55596.793	8.681, 38.675	
	5%, 95%	8166.693, 55596.793	8.681, 38.675	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 248 of 264)

Biomarker: Trans-3-hydroxycotinine (pg/24hr)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	8	0.0024
	MEAN, GEO MEAN	5244.516, 4694.147	5.332, 4.000	
	SD, SE	2502.1057, 1021.4804	3.8207, 1.3508	
	MEDIAN	5103.109	4.567	
	MIN, MAX	1903.535, 9111.993	1.130, 10.869	
	5%, 95%	1903.535, 9111.993	1.130, 10.869	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	5531.660, 4530.332	5.153, 4.393	
	SD, SE	4010.1922, 1637.1541	3.0018, 1.1346	
	MEDIAN	4750.098	4.444	
	MIN, MAX	1741.810, 13031.000	2.059, 9.197	
	5%, 95%	1741.810, 13031.000	2.059, 9.197	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	3975.535, 3052.302	4.239, 3.763	
	SD, SE	3446.6359, 1541.3824	2.2143, 0.9903	
	MEDIAN	2673.601	3.503	
	MIN, MAX	1063.570, 9914.118	1.816, 6.991	
	5%, 95%	1063.570, 9914.118	1.816, 6.991	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	5050.920, 4284.770	4.526, 3.792	
	SD, SE	3168.8595, 1293.6815	2.5804, 0.9123	
	MEDIAN	4158.453	4.752	
	MIN, MAX	1569.638, 10685.704	1.668, 7.433	
	5%, 95%	1569.638, 10685.704	1.668, 7.433	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 249 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	NA
	MEAN, GEO MEAN	1560.823, 1486.474	
	SD, SE	503.6919, 205.6314	
	MEDIAN	1524.586	
	MIN, MAX	786.539, 2370.446	
	5%, 95%	786.539, 2370.446	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	NA
	MEAN, GEO MEAN	2176.587, 1786.231	
	SD, SE	1569.9617, 640.9342	
	MEDIAN	1465.382	
	MIN, MAX	906.249, 4801.595	
	5%, 95%	906.249, 4801.595	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	NA
	MEAN, GEO MEAN	1617.681, 1453.841	
	SD, SE	790.0583, 353.3248	
	MEDIAN	1585.017	
	MIN, MAX	772.806, 2579.115	
	5%, 95%	772.806, 2579.115	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	NA
	MEAN, GEO MEAN	1781.061, 1665.949	
	SD, SE	729.6039, 297.8596	
	MEDIAN	1518.531	
	MIN, MAX	1103.963, 2779.840	
	5%, 95%	1103.963, 2779.840	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((µg/24hr)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	299.990, 283.700		
	SD, SE	96.8096, 39.5224		
	MEDIAN	293.026		
	MIN, MAX	151.173, 455.600		
	5%, 95%	151.173, 455.600		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	418.340, 343.314		
	SD, SE	301.7467, 123.1876		
	MEDIAN	281.646		
	MIN, MAX	174.181, 922.867		
	5%, 95%	174.181, 922.867		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	310.918, 279.428		
	SD, SE	151.8493, 67.9091		
	MEDIAN	304.640		
	MIN, MAX	148.533, 495.706		
	5%, 95%	148.533, 495.706		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6		NA
	MEAN, GEO MEAN	342.320, 320.195		
	SD, SE	140.2297, 57.2485		
	MEDIAN	291.862		
	MIN, MAX	212.182, 534.285		
	5%, 95%	212.182, 534.285		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 251 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	8	0.0024
	MEAN, GEO MEAN	21.591, 17.695	0.018, 0.014	
	SD, SE	17.3519, 7.0839	0.0129, 0.0046	
	MEDIAN	16.395	0.014	
	MIN, MAX	8.155, 55.986	0.005, 0.041	
	5%, 95%	8.155, 55.986	0.005, 0.041	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	23.863, 18.574	0.016, 0.015	
	SD, SE	22.4716, 9.1740	0.0066, 0.0025	
	MEDIAN	15.847	0.017	
	MIN, MAX	9.465, 68.993	0.008, 0.024	
	5%, 95%	9.465, 68.993	0.008, 0.024	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0119
	MEAN, GEO MEAN	19.402, 15.516	0.018, 0.015	
	SD, SE	17.0839, 7.6401	0.0108, 0.0048	
	MEDIAN	12.774	0.016	
	MIN, MAX	9.346, 49.656	0.008, 0.032	
	5%, 95%	9.346, 49.656	0.008, 0.032	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	21.660, 17.595	0.016, 0.013	
	SD, SE	18.2969, 7.4697	0.0094, 0.0033	
	MEDIAN	15.202	0.014	
	MIN, MAX	9.166, 58.212	0.005, 0.032	
	5%, 95%	9.166, 58.212	0.005, 0.032	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 252 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	8	0.0023
	MEAN, GEO MEAN	4.150, 3.401	0.003, 0.003	
	SD, SE	3.3353, 1.3616	0.0025, 0.0009	
	MEDIAN	3.151	0.003	
	MIN, MAX	1.567, 10.761	0.001, 0.008	
	5%, 95%	1.567, 10.761	0.001, 0.008	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0032
	MEAN, GEO MEAN	4.586, 3.570	0.003, 0.003	
	SD, SE	4.3189, 1.7632	0.0012, 0.0005	
	MEDIAN	3.046	0.003	
	MIN, MAX	1.819, 13.260	0.002, 0.005	
	5%, 95%	1.819, 13.260	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0119
	MEAN, GEO MEAN	3.729, 2.982	0.004, 0.003	
	SD, SE	3.2837, 1.4685	0.0018, 0.0008	
	MEDIAN	2.455	0.003	
	MIN, MAX	1.796, 9.544	0.002, 0.006	
	5%, 95%	1.796, 9.544	0.002, 0.006	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	4.163, 3.382	0.003, 0.003	
	SD, SE	3.5166, 1.4356	0.0016, 0.0006	
	MEDIAN	2.922	0.003	
	MIN, MAX	1.761, 11.188	0.001, 0.006	
	5%, 95%	1.761, 11.188	0.001, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 253 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine)/cigarette per day			Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6		NA
	MEAN, GEO MEAN	1.241, 1.077		
	SD, SE	0.8099, 0.3306		
	MEDIAN	0.966		
	MIN, MAX	0.560, 2.799		
	5%, 95%	0.560, 2.799		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1.719, 1.408		
	SD, SE	1.2049, 0.4919		
	MEDIAN	1.126		
	MIN, MAX	0.623, 3.450		
	5%, 95%	0.623, 3.450		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	1.611, 1.420		
	SD, SE	0.7635, 0.3415		
	MEDIAN	1.646		
	MIN, MAX	0.519, 2.483		
	5%, 95%	0.519, 2.483		
	# of BLQ/ALQ Values	0/0		
Overall†	N	6		NA
	MEAN, GEO MEAN	1.486, 1.321		
	SD, SE	0.8156, 0.3330		
	MEDIAN	1.255		
	MIN, MAX	0.645, 2.911		
	5%, 95%	0.645, 2.911		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 254 of 264)

Biomarker: Trans-3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6		NA
	MEAN, GEO MEAN	0.239, 0.207		
	SD, SE	0.1555, 0.0635		
	MEDIAN	0.186		
	MIN, MAX	0.108, 0.538		
	5%, 95%	0.108, 0.538		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.330, 0.271		
	SD, SE	0.2315, 0.0945		
	MEDIAN	0.217		
	MIN, MAX	0.120, 0.663		
	5%, 95%	0.120, 0.663		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.310, 0.273		
	SD, SE	0.1466, 0.0655		
	MEDIAN	0.316		
	MIN, MAX	0.100, 0.477		
	5%, 95%	0.100, 0.477		
	# of BLQ/ALQ Values	0/0		
Overall [*]	N	6		NA
	MEAN, GEO MEAN	0.286, 0.254		
	SD, SE	0.1565, 0.0639		
	MEDIAN	0.241		
	MIN, MAX	0.124, 0.559		
	5%, 95%	0.124, 0.559		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (nmol/L)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*
Week 1	N	6	8	0.0024
	MEAN, GEO MEAN	15531.5, 14510.3	12.9, 10.0	
	SD, SE	5703.03, 2328.25	9.94, 3.51	
	MEDIAN	16253.2	8.3	
	MIN, MAX	7282.3, 21708.6	4.9, 31.9	
	5%, 95%	7282.3, 21708.6	4.9, 31.9	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	16215.6, 13989.4	12.7, 10.9	
	SD, SE	8993.85, 3671.72	7.86, 2.97	
	MEDIAN	14730.5	10.3	
	MIN, MAX	5006.9, 30541.0	6.0, 27.6	
	5%, 95%	5006.9, 30541.0	6.0, 27.6	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0122
	MEAN, GEO MEAN	10483.2, 8939.9	11.3, 10.7	
	SD, SE	6664.13, 2980.29	4.09, 1.83	
	MEDIAN	8860.2	12.4	
	MIN, MAX	4009.9, 21054.0	7.0, 16.9	
	5%, 95%	4009.9, 21054.0	7.0, 16.9	
	# of BLQ/ALQ Values	0/0	0/0	
Overall*	N	6	8	0.0024
	MEAN, GEO MEAN	14945.7, 13284.5	11.3, 10.0	
	SD, SE	7410.05, 3025.14	6.05, 2.14	
	MEDIAN	14143.7	10.6	
	MIN, MAX	5433.0, 26124.8	5.5, 22.2	
	5%, 95%	5433.0, 26124.8	5.5, 22.2	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 256 of 264)

Biomarker: Trans-3-hydroxycotinine (ng/mL)		Analytical Lab: INBIFO		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	8	0.0024
	MEAN, GEO MEAN	2985.2, 2788.9	2.5, 1.9	
	SD, SE	1096.11, 447.48	1.92, 0.68	
	MEDIAN	3123.9	1.6	
	MIN, MAX	1399.7, 4172.4	0.9, 6.1	
	5%, 95%	1399.7, 4172.4	0.9, 6.1	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	7	0.0034
	MEAN, GEO MEAN	3116.6, 2688.7	2.4, 2.1	
	SD, SE	1728.63, 705.71	1.50, 0.57	
	MEDIAN	2831.2	2.0	
	MIN, MAX	962.3, 5870.0	1.2, 5.3	
	5%, 95%	962.3, 5870.0	1.2, 5.3	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5	5	0.0119
	MEAN, GEO MEAN	2014.9, 1718.2	2.1, 2.0	
	SD, SE	1280.85, 572.81	0.79, 0.35	
	MEDIAN	1702.9	2.4	
	MIN, MAX	770.7, 4046.6	1.3, 3.2	
	5%, 95%	770.7, 4046.6	1.3, 3.2	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	6	8	0.0024
	MEAN, GEO MEAN	2872.6, 2553.3	2.2, 1.9	
	SD, SE	1424.22, 581.44	1.15, 0.40	
	MEDIAN	2718.4	2.0	
	MIN, MAX	1044.2, 5021.2	1.1, 4.2	
	5%, 95%	1044.2, 5021.2	1.1, 4.2	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 257 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	992.0, 883.1		
	SD, SE	474.97, 193.91		
	MEDIAN	920.8		
	MIN, MAX	321.0, 1758.1		
	5%, 95%	321.0, 1758.1		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	1222.6, 1060.1		
	SD, SE	663.49, 270.87		
	MEDIAN	1276.8		
	MIN, MAX	500.7, 2233.3		
	5%, 95%	500.7, 2233.3		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	854.5, 818.4		
	SD, SE	258.22, 115.48		
	MEDIAN	1022.6		
	MIN, MAX	492.2, 1052.7		
	5%, 95%	492.2, 1052.7		
	# of BLQ/ALQ Values	0/0		
Overall ^a	N	6		NA
	MEAN, GEO MEAN	1044.2, 1007.3		
	SD, SE	292.56, 119.44		
	MEDIAN	1092.5		
	MIN, MAX	636.9, 1413.6		
	5%, 95%	636.9, 1413.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 258 of 264)

Biomarker: Trans-3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: TNBIFO		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	190.7, 169.7		
	SD, SE	91.29, 37.27		
	MEDIAN	177.0		
	MIN, MAX	61.7, 337.9		
	5%, 95%	61.7, 337.9		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	235.0, 203.8		
	SD, SE	127.51, 52.06		
	MEDIAN	245.4		
	MIN, MAX	96.2, 429.2		
	5%, 95%	96.2, 429.2		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	164.2, 157.3		
	SD, SE	49.61, 22.19		
	MEDIAN	196.5		
	MIN, MAX	94.6, 202.3		
	5%, 95%	94.6, 202.3		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6		NA
	MEAN, GEO MEAN	200.7, 193.6		
	SD, SE	56.23, 22.96		
	MEDIAN	210.0		
	MIN, MAX	122.4, 271.7		
	5%, 95%	122.4, 271.7		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 259 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/L) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	3229.3, 2944.6	18.1, 17.2	
	SD, SE	1244.01, 507.87	7.71, 5.45	
	MEDIAN	3884.0	18.1	
	MIN, MAX	1134.7, 4122.8	12.6, 23.5	
	5%, 95%	1134.7, 4122.8	12.6, 23.5	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	1	NA
	MEAN, GEO MEAN	3761.5, 3336.9	14.3, 14.3	
	SD, SE	2090.68, 853.52	NA, NA	
	MEDIAN	2948.4	14.3	
	MIN, MAX	1937.9, 7148.3	14.3, 14.3	
	5%, 95%	1937.9, 7148.3	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5		NA
	MEAN, GEO MEAN	2442.3, 1338.9		
	SD, SE	2744.27, 1227.28		
	MEDIAN	1240.5		
	MIN, MAX	270.0, 6900.4		
	5%, 95%	270.0, 6900.4		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6	2	0.0668
	MEAN, GEO MEAN	3314.7, 2908.5	18.5, 17.8	
	SD, SE	1730.35, 706.41	7.07, 5.00	
	MEDIAN	3199.8	18.5	
	MIN, MAX	1319.5, 5509.1	13.5, 23.5	
	5%, 95%	1319.5, 5509.1	13.5, 23.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234^a will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 260 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	197.4, 179.2	
	SD, SE	83.47, 34.08	
	MEDIAN	196.9	
	MIN, MAX	68.4, 324.8	
	5%, 95%	68.4, 324.8	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	
	MEAN, GEO MEAN	288.2, 252.9	
	SD, SE	144.58, 59.02	
	MEDIAN	306.4	
	MIN, MAX	96.9, 494.5	
	5%, 95%	96.9, 494.5	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	
	MEAN, GEO MEAN	179.5, 122.6	
	SD, SE	137.74, 61.60	
	MEDIAN	206.8	
	MIN, MAX	32.1, 345.0	
	5%, 95%	32.1, 345.0	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	
	MEAN, GEO MEAN	226.3, 213.1	
	SD, SE	84.55, 34.52	
	MEDIAN	225.0	
	MIN, MAX	119.3, 362.6	
	5%, 95%	119.3, 362.6	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/24hr)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	5915.230, 4956.210	46.567, 35.776	
	SD, SE	3528.2682, 1440.4094	42.1556, 29.8085	
	MEDIAN	5879.115	46.567	
	MIN, MAX	1543.192, 11872.310	16.758, 76.375	
	5%, 95%	1543.192, 11872.310	16.758, 76.375	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	1	NA
	MEAN, GEO MEAN	5976.365, 5622.441	24.024, 24.024	
	SD, SE	2460.4198, 1004.4622	NA, NA	
	MEDIAN	4840.694	24.024	
	MIN, MAX	3837.042, 10362.680	24.024, 24.024	
	5%, 95%	3837.042, 10362.680	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5		NA
	MEAN, GEO MEAN	5169.565, 2378.384		
	SD, SE	6804.7412, 3043.1728		
	MEDIAN	2667.075		
	MIN, MAX	372.600, 16905.980		
	5%, 95%	372.600, 16905.980		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	6	2	0.0668
	MEAN, GEO MEAN	5777.447, 4931.565	48.383, 39.463	
	SD, SE	3856.0276, 1574.2167	39.5867, 27.9920	
	MEDIAN	4375.768	48.383	
	MIN, MAX	2179.450, 13046.990	20.391, 76.375	
	5%, 95%	2179.450, 13046.990	20.391, 76.375	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 262 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO	
Timepoint	Statistic	Smokers	Non-Smokers
Week 1	N	6	
	MEAN, GEO MEAN	326.104, 301.650	
	SD, SE	148.2217, 60.5112	
	MEDIAN	276.753	
	MIN, MAX	167.506, 593.616	
	5%, 95%	167.506, 593.616	
	# of BLQ/ALQ Values	0/0	
Week 2	N	6	
	MEAN, GEO MEAN	461.555, 426.075	
	SD, SE	189.3290, 77.2932	
	MEDIAN	461.075	
	MIN, MAX	191.852, 769.055	
	5%, 95%	191.852, 769.055	
	# of BLQ/ALQ Values	0/0	
Week 3	N	5	
	MEAN, GEO MEAN	363.714, 217.734	
	SD, SE	328.0110, 146.6910	
	MEDIAN	416.278	
	MIN, MAX	50.380, 845.299	
	5%, 95%	50.380, 845.299	
	# of BLQ/ALQ Values	0/0	
Overall*	N	6	
	MEAN, GEO MEAN	381.335, 355.488	
	SD, SE	159.8954, 65.2770	
	MEDIAN	352.888	
	MIN, MAX	209.009, 652.350	
	5%, 95%	209.009, 652.350	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 263 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine) Analytical Lab: INBIFO				
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	6	2	0.0668
	MEAN, GEO MEAN	4.796, 3.591	0.031, 0.020	
	SD, SE	4.6266, 1.8888	0.0339, 0.0240	
	MEDIAN	3.582	0.031	
	MIN, MAX	1.271, 14.020	0.007, 0.055	
	5%, 95%	1.271, 14.020	0.007, 0.055	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	6	1	NA
	MEAN, GEO MEAN	4.998, 4.431	0.009, 0.009	
	SD, SE	2.9163, 1.1906	NA, NA	
	MEDIAN	4.687	0.009	
	MIN, MAX	2.318, 10.545	0.009, 0.009	
	5%, 95%	2.318, 10.545	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	5		NA
	MEAN, GEO MEAN	4.826, 2.324		
	SD, SE	6.5574, 2.9326		
	MEDIAN	2.547		
	MIN, MAX	0.609, 16.275		
	5%, 95%	0.609, 16.275		
	# of BLQ/ALQ Values	0/0		
Overall*	N	6	2	0.0668
	MEAN, GEO MEAN	4.837, 3.842	0.032, 0.021	
	SD, SE	4.3685, 1.7834	0.0332, 0.0235	
	MEDIAN	3.397	0.032	
	MIN, MAX	2.192, 13.613	0.008, 0.055	
	5%, 95%	2.192, 13.613	0.008, 0.055	

^a P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 264 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	6		NA
	MEAN, GEO MEAN	0.265, 0.219		
	SD, SE	0.2168, 0.0885		
	MEDIAN	0.201		
	MIN, MAX	0.119, 0.701		
	5%, 95%	0.119, 0.701		
	# of BLQ/ALQ Values	0/0		
Week 2	N	6		NA
	MEAN, GEO MEAN	0.378, 0.336		
	SD, SE	0.1636, 0.0668		
	MEDIAN	0.449		
	MIN, MAX	0.116, 0.527		
	5%, 95%	0.116, 0.527		
	# of BLQ/ALQ Values	0/0		
Week 3	N	5		NA
	MEAN, GEO MEAN	0.344, 0.213		
	SD, SE	0.3074, 0.1375		
	MEDIAN	0.336		
	MIN, MAX	0.034, 0.814		
	5%, 95%	0.034, 0.814		
	# of BLQ/ALQ Values	0/0		
Overall ^a	N	6		NA
	MEAN, GEO MEAN	0.321, 0.278		
	SD, SE	0.1946, 0.0795		
	MEDIAN	0.293		
	MIN, MAX	0.118, 0.681		
	5%, 95%	0.118, 0.681		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 8)

Biomarker: Acetonitrile (nL/L @20 °C and 1 atm)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	0.0020
	MEAN, GEO MEAN	12771.286, 2830.905	23024.374, 9604.280	
	SD, SE	16174.6257, 2287.4375	20647.3178, 2560.9846	
	MEDIAN	7559.747	19298.217	
	MIN, MAX	27.047, 61266.718	27.047, 90418.051	
	5%, 95%	27.047, 43336.359	92.902, 54497.370	
	# of BLQ/ALQ Values	3/12	2/0	
Week 3	N	46	65	0.0003
	MEAN, GEO MEAN	14740.147, 4167.738	25525.906, 16294.636	
	SD, SE	15322.4372, 2259.1701	15334.1170, 1901.9631	
	MEDIAN	11061.267	25973.434	
	MIN, MAX	27.047, 55212.198	27.047, 64440.436	
	5%, 95%	360.626, 41797.811	571.554, 48358.890	
	# of BLQ/ALQ Values	1/14	1/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	13484.527, 3570.907	25638.963, 17780.694	
	SD, SE	15300.2649, 2360.8821	13884.4733, 1722.1570	
	MEDIAN	6200.319	28505.088	
	MIN, MAX	27.047, 57117.622	143.554, 58955.534	
	5%, 95%	360.626, 38261.231	2225.726, 46880.251	
	# of BLQ/ALQ Values	2/12	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	14217.256, 5394.281	24729.748, 21455.756	
	SD, SE	13608.7604, 1924.5694	11459.6009, 1421.3886	
	MEDIAN	13301.411	24283.147	
	MIN, MAX	138.408, 61266.718	2561.353, 52452.649	
	5%, 95%	249.433, 41598.061	6272.987, 39744.215	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 8)

Biomarker: Acetonitrile (nmol/L)		Analytical Lab: Madison		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	0.0020
	MEAN, GEO MEAN	530.898, 117.677	957.116, 399.243	
	SD, SE	672.3739, 95.0880	858.3023, 106.4593	
	MEDIAN	314.257	802.221	
	MIN, MAX	1.124, 2546.837	1.124, 3758.649	
	5%, 95%	1.124, 1801.478	3.862, 2265.438	
	# of BLQ/ALQ Values	3/12	2/0	
Week 3	N	46	65	0.0003
	MEAN, GEO MEAN	612.743, 173.250	1061.103, 677.359	
	SD, SE	636.9487, 93.9130	637.4342, 79.0640	
	MEDIAN	459.814	1079.707	
	MIN, MAX	1.124, 2295.153	1.124, 2678.768	
	5%, 95%	14.991, 1737.521	23.759, 2010.263	
	# of BLQ/ALQ Values	1/14	1/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	560.547, 148.439	1065.803, 739.139	
	SD, SE	636.0270, 98.1411	577.1730, 71.5895	
	MEDIAN	257.745	1184.947	
	MIN, MAX	1.124, 2374.361	5.968, 2450.762	
	5%, 95%	14.991, 1590.507	92.523, 1948.797	
	# of BLQ/ALQ Values	2/12	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	591.007, 224.238	1028.007, 891.909	
	SD, SE	565.7117, 80.0037	476.3719, 59.0867	
	MEDIAN	552.935	1009.442	
	MIN, MAX	5.753, 2546.837	106.475, 2180.439	
	5%, 95%	10.369, 1729.218	260.766, 1652.154	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 8)

Biomarker: Acetonitrile ((nL/L @20 °C and 1 arm)cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	1086.236, 217.463		
	SD, SE	2682.8000, 379.4052		
	MEDIAN	546.023		
	MIN, MAX	1.378, 18842.877		
	5%, 95%	2.254, 2802.105		
	# of BLQ/ALQ Values	3/12		
Week 3	N	46		NA
	MEAN, GEO MEAN	1430.704, 332.223		
	SD, SE	2317.4116, 341.6837		
	MEDIAN	833.470		
	MIN, MAX	1.803, 13126.227		
	5%, 95%	18.031, 5639.894		
	# of BLQ/ALQ Values	1/14		
Week 6	N	42		NA
	MEAN, GEO MEAN	1495.642, 267.395		
	SD, SE	3294.4494, 508.3446		
	MEDIAN	378.483		
	MIN, MAX	1.352, 19039.207		
	5%, 95%	14.425, 5729.977		
	# of BLQ/ALQ Values	2/12		
Overall [*]	N	50		NA
	MEAN, GEO MEAN	1355.640, 435.265		
	SD, SE	1920.0254, 271.5326		
	MEDIAN	877.738		
	MIN, MAX	6.920, 11017.118		
	5%, 95%	15.627, 4456.056		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 8)

Biomarker: Acetonitrile ((nmol/L)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	45.154, 9.039		
	SD, SE	111.5231, 15.7717		
	MEDIAN	22.698		
	MIN, MAX	0.057, 783.292		
	5%, 95%	0.094, 116.483		
	# of BLQ/ALQ Values	3/12		
Week 3	N	46		NA
	MEAN, GEO MEAN	59.474, 13.812		
	SD, SE	96.3340, 14.2037		
	MEDIAN	34.647		
	MIN, MAX	0.075, 545.653		
	5%, 95%	0.750, 234.449		
	# of BLQ/ALQ Values	1/14		
Week 6	N	42		NA
	MEAN, GEO MEAN	62.173, 11.116		
	SD, SE	136.9492, 21.1317		
	MEDIAN	15.734		
	MIN, MAX	0.056, 791.454		
	5%, 95%	0.600, 238.193		
	# of BLQ/ALQ Values	2/12		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	56.354, 18.095		
	SD, SE	79.8149, 11.2875		
	MEDIAN	36.487		
	MIN, MAX	0.288, 457.978		
	5%, 95%	0.650, 185.237		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhaled Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Acetonitrile (ng/mL)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50	65	0.0020
	MEAN, GEO MEAN	3541422.49, 784997.78	6384359.49, 2663225.25	
	SD, SE	4485153.910, 634296.549	5725412.124, 710149.973	
	MEDIAN	2096285.14	5351312.21	
	MIN, MAX	7500.00, 16988996.62	7500.00, 25072535.47	
	5%, 95%	7500.00, 12016985.39	25761.32, 15111885.45	
	# of BLQ/ALQ Values	3/12	2/0	
Week 3	N	46	65	0.0003
	MEAN, GEO MEAN	4087379.02, 1155695.46	7078223.49, 4518431.88	
	SD, SE	4248845.728, 626458.126	4252084.490, 527406.171	
	MEDIAN	3067241.42	7202321.10	
	MIN, MAX	7500.00, 15310104.26	7500.00, 17869054.85	
	5%, 95%	100000.00, 11590352.68	158489.34, 13409711.46	
	# of BLQ/ALQ Values	1/14	1/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	3739201.06, 990196.87	7109573.85, 4930509.83	
	SD, SE	4242697.448, 654662.429	3850104.529, 477546.693	
	MEDIAN	1719321.63	7904337.84	
	MIN, MAX	7500.00, 15838470.03	39806.96, 16348115.24	
	5%, 95%	100000.00, 10609674.23	617184.22, 12999691.34	
	# of BLQ/ALQ Values	2/12	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	3942383.60, 1495810.65	6857452.28, 5949588.46	
	SD, SE	3773650.566, 533674.781	3177697.892, 394144.915	
	MEDIAN	3688423.85	6733611.88	
	MIN, MAX	38379.95, 16988996.62	710251.93, 14544893.17	
	5%, 95%	69166.67, 11534962.73	1739472.33, 11020899.43	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhaled Biomarkers of Exposure by Timepoint and Overall
(Page 6 of 8)

Biomarker: Acetonitrile ((ng/mL)/cigarette per day)		Analytical Lab: Madison		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	301208.44, 60301.04		
	SD, SE	743928.886, 105207.432		
	MEDIAN	151409.90		
	MIN, MAX	381.99, 5225048.61		
	5%, 95%	625.00, 777011.51		
	# of BLQ/ALQ Values	3/12		
Week 3	N	46		NA
	MEAN, GEO MEAN	396728.13, 92124.35		
	SD, SE	642608.244, 94747.417		
	MEDIAN	231117.50		
	MIN, MAX	500.00, 3639846.15		
	5%, 95%	5000.00, 1563918.26		
	# of BLQ/ALQ Values	1/14		
Week 6	N	42		NA
	MEAN, GEO MEAN	414735.01, 74148.18		
	SD, SE	913536.611, 140961.759		
	MEDIAN	104951.71		
	MIN, MAX	375.00, 5279490.01		
	5%, 95%	4000.00, 1588897.93		
	# of BLQ/ALQ Values	2/12		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	375913.22, 120697.61		
	SD, SE	532414.763, 75294.818		
	MEDIAN	243392.79		
	MIN, MAX	1919.00, 3054999.42		
	5%, 95%	4333.33, 1235645.07		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 7 of 8)

Biomarker: Carbon monoxide (ppm)		Analytical Lab: CRF		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a
Week 1	N	50	65	<.0001
	MEAN, GEO MEAN	26.3, 22.5	5.7, 5.5	
	SD, SE	14.89, 2.11	1.35, 0.17	
	MEDIAN	23.5	5.7	
	MIN, MAX	7.8, 71.4	3.6, 9.6	
	5%, 95%	8.6, 54.7	3.7, 8.1	
	# of BLQ/ALQ Values	0/0	0/0	
Week 2	N	49	65	<.0001
	MEAN, GEO MEAN	24.5, 20.3	3.1, 4.7	
	SD, SE	15.54, 2.22	1.60, 0.20	
	MEDIAN	21.2	5.2	
	MIN, MAX	4.5, 88.9	0.1, 9.6	
	5%, 95%	6.7, 50.1	3.2, 7.7	
	# of BLQ/ALQ Values	0/0	0/0	
Week 3	N	46	65	<.0001
	MEAN, GEO MEAN	26.3, 22.3	5.2, 4.9	
	SD, SE	14.50, 2.14	1.65, 0.20	
	MEDIAN	23.7	5.2	
	MIN, MAX	5.3, 62.2	0.3, 10.6	
	5%, 95%	7.2, 55.1	3.2, 8.3	
	# of BLQ/ALQ Values	0/0	0/0	
Week 6	N	42	65	<.0001
	MEAN, GEO MEAN	29.2, 25.0	6.2, 5.6	
	SD, SE	14.61, 2.25	2.44, 0.30	
	MEDIAN	27.0	5.8	
	MIN, MAX	4.0, 70.5	0.4, 13.8	
	5%, 95%	10.0, 51.1	3.6, 11.6	
	# of BLQ/ALQ Values	0/0	0/0	
Overall ^b	N	50	65	<.0001
	MEAN, GEO MEAN	26.2, 22.5	5.6, 5.5	
	SD, SE	14.18, 2.00	1.17, 0.15	
	MEDIAN	22.1	5.3	
	MIN, MAX	5.9, 66.0	3.1, 8.6	
	5%, 95%	9.5, 49.2	3.7, 7.8	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439143

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-3
Statistical Comparison Between Smokers and Non-Smokers of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 8)

Biomarker: Carbon monoxide ((ppm)/cigarette per day)		Analytical Lab: CRF		P-value*
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	2.2, 1.7		
	SD, SE	2.26, 0.32		
	MEDIAN	1.6		
	MIN, MAX	0.5, 14.3		
	5%, 95%	0.6, 5.0		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	2.3, 1.6		
	SD, SE	3.16, 0.45		
	MEDIAN	1.5		
	MIN, MAX	0.5, 22.1		
	5%, 95%	0.7, 4.9		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	2.1, 1.8		
	SD, SE	1.66, 0.25		
	MEDIAN	1.7		
	MIN, MAX	0.6, 11.0		
	5%, 95%	0.8, 5.2		
	# of BLQ/ALQ Values	0/0		
Week 6	N	42		NA
	MEAN, GEO MEAN	2.8, 1.9		
	SD, SE	5.31, 0.82		
	MEDIAN	1.8		
	MIN, MAX	0.6, 35.3		
	5%, 95%	0.9, 6.8		
	# of BLQ/ALQ Values	0/0		
Overall†	N	50		NA
	MEAN, GEO MEAN	2.3, 1.8		
	SD, SE	2.83, 0.40		
	MEDIAN	1.8		
	MIN, MAX	0.6, 20.7		
	5%, 95%	0.8, 5.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

† Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439144

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 9)

Biomarker: Carboxyhemoglobin (% saturation) Analytical Lab: CCLS

Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Female	Week 1	N	24	8	0.7938	23	12	0.5293
		MEAN, GEO MEAN	4.3, 3.3	4.9, 3.4		0.3, 0.3	0.3, 0.3	
		SD, SE	2.85, 0.58	3.84, 1.36		0.09, 0.02	0.06, 0.02	
		MEDIAN	3.2	4.5		0.3	0.3	
		MIN, MAX	0.8, 11.3	0.9, 11.4		0.3, 0.7	0.3, 0.5	
		5%, 95%	0.9, 8.9	0.9, 11.4		0.3, 0.4	0.3, 0.5	
		# of BLQ/ALQ Values	0/0	0/0		18/0	9/0	
	Week 2	N	22	9	0.3838	27	8	0.8869
		MEAN, GEO MEAN	4.4, 3.1	3.5, 2.2		0.3, 0.3	0.3, 0.3	
		SD, SE	3.33, 0.71	2.99, 1.00		0.05, 0.01	0.07, 0.03	
		MEDIAN	4.7	2.6		0.3	0.3	
		MIN, MAX	0.3, 13.3	0.3, 9.8		0.3, 0.5	0.3, 0.5	
		5%, 95%	0.6, 10.1	0.3, 9.8		0.3, 0.4	0.3, 0.5	
		# of BLQ/ALQ Values	1/0	1/0		23/0	7/0	
	Week 3	N	24	5	0.2143	28	7	0.0468
		MEAN, GEO MEAN	5.0, 4.1	3.7, 2.7		0.4, 0.4	0.7, 0.5	
		SD, SE	2.70, 0.55	3.19, 1.43		0.43, 0.08	0.81, 0.31	
		MEDIAN	4.3	3.1		0.3	0.4	
		MIN, MAX	0.3, 9.7	0.7, 9.1		0.3, 2.2	0.3, 2.5	
		5%, 95%	1.3, 9.3	0.7, 9.1		0.3, 1.6	0.3, 2.5	
		# of BLQ/ALQ Values	0/0	0/0		20/0	2/0	
	Week 6	N	22	6	0.6340	30	5	0.0544
		MEAN, GEO MEAN	4.7, 3.9	4.3, 2.4		0.4, 0.3	0.5, 0.4	
		SD, SE	2.41, 0.51	3.91, 1.60		0.21, 0.04	0.18, 0.08	
		MEDIAN	4.7	3.4		0.3	0.4	
		MIN, MAX	0.4, 9.8	0.3, 9.2		0.3, 1.3	0.3, 0.7	
		5%, 95%	1.0, 8.2	0.3, 9.2		0.3, 0.8	0.3, 0.7	
		# of BLQ/ALQ Values	0/0	1/0		21/0	1/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

PM3006439145

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 9)

Biomarker: Carboxyhemoglobin (% saturation) Analytical Lab: CCLS

Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value*	AM	PM	P-value*
Male	Week 1	N	10	8	0.7895	20	10	0.7820
		MEAN, GEO MEAN	4.9, 3.4	3.7, 3.1		0.5, 0.4	0.5, 0.4	
		SD, SE	4.10, 1.30	2.16, 0.76		0.21, 0.05	0.20, 0.06	
		MEDIAN	4.1	3.5		0.4	0.4	
		MIN, MAX	0.3, 14.8	0.9, 7.9		0.3, 1.0	0.3, 0.8	
		5%, 95%	0.3, 14.8	0.9, 7.9		0.3, 0.9	0.3, 0.8	
		# of BLQ/ALQ Values	1/0	0/0		7/0	5/0	
	Week 2	N	12	6	0.8883	24	6	0.7107
		MEAN, GEO MEAN	3.7, 2.6	3.8, 3.0		0.4, 0.4	0.5, 0.4	
		SD, SE	2.77, 0.80	2.79, 1.14		0.18, 0.04	0.35, 0.14	
		MEDIAN	3.0	3.5		0.3	0.3	
		MIN, MAX	0.3, 8.6	1.0, 8.4		0.3, 0.9	0.3, 1.1	
		5%, 95%	0.3, 8.6	1.0, 8.4		0.3, 0.8	0.3, 1.1	
		# of BLQ/ALQ Values	1/0	0/0		14/0	3/0	
	Week 3	N	13	4	0.8207	23	7	0.8679
		MEAN, GEO MEAN	4.5, 3.1	5.5, 4.3		0.5, 0.4	0.4, 0.4	
		SD, SE	3.47, 0.96	4.08, 2.04		0.53, 0.11	0.17, 0.06	
		MEDIAN	3.8	4.8		0.3	0.3	
		MIN, MAX	0.3, 11.3	1.8, 10.5		0.3, 2.8	0.3, 0.7	
		5%, 95%	0.3, 11.3	1.8, 10.5		0.3, 1.0	0.3, 0.7	
		# of BLQ/ALQ Values	1/0	0/0		13/0	3/0	
	Week 6	N	9	4	0.3961	24	6	0.1665
		MEAN, GEO MEAN	5.5, 3.8	3.5, 3.1		0.4, 0.4	0.6, 0.5	
		SD, SE	4.02, 1.34	1.87, 0.94		0.16, 0.03	0.31, 0.13	
		MEDIAN	4.5	3.3		0.3	0.5	
		MIN, MAX	0.3, 13.9	1.5, 5.8		0.3, 0.9	0.3, 1.1	
		5%, 95%	0.3, 13.9	1.5, 5.8		0.3, 0.7	0.3, 1.1	
		# of BLQ/ALQ Values	1/0	0/0		10/0	2/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

* P-value from Wilcoxon rank-sum test.

PM3006439146

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 9)

Biomarker: Carboxyhemoglobin (% saturation) Analytical Lab: CCLS

Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Overall	Week 1	N	34	16	0.9585	43	22	0.9400
		MEAN, GEO MEAN	4.5, 3.3	4.3, 3.3		0.4, 0.4	0.4, 0.4	
		SD, SE	3.21, 0.55	3.08, 0.77		0.17, 0.03	0.16, 0.03	
		MEDIAN	3.7	4.2		0.3	0.3	
		MIN, MAX	0.3, 14.8	0.9, 11.4		0.3, 1.0	0.3, 0.8	
		5%, 95%	0.8, 11.3	0.9, 11.4		0.3, 0.7	0.3, 0.7	
		# of BLQ/ALQ Values	1/0	0/0		25/0	14/0	
	Week 2	N	34	15	0.5875	51	14	0.8503
		MEAN, GEO MEAN	4.2, 2.9	3.6, 2.5		0.4, 0.3	0.4, 0.4	
		SD, SE	3.12, 0.54	2.81, 0.73		0.13, 0.02	0.24, 0.07	
		MEDIAN	3.6	2.6		0.3	0.3	
		MIN, MAX	0.3, 13.3	0.3, 9.8		0.3, 0.9	0.3, 1.1	
		5%, 95%	0.3, 10.1	0.3, 9.8		0.3, 0.7	0.3, 1.1	
		# of BLQ/ALQ Values	2/0	1/0		37/0	10/0	
	Week 3	N	37	9	0.4974	51	14	0.1438
		MEAN, GEO MEAN	4.8, 3.7	4.5, 3.3		0.5, 0.4	0.6, 0.4	
		SD, SE	2.96, 0.49	3.49, 1.16		0.48, 0.07	0.58, 0.16	
		MEDIAN	4.1	3.1		0.3	0.4	
		MIN, MAX	0.3, 11.3	0.7, 10.5		0.3, 2.8	0.3, 2.5	
		5%, 95%	0.3, 10.4	0.7, 10.5		0.3, 1.6	0.3, 2.5	
		# of BLQ/ALQ Values	1/0	0/0		33/0	5/0	
	Week 6	N	31	10	0.3387	54	11	0.0194
		MEAN, GEO MEAN	4.9, 3.8	4.0, 2.7		0.4, 0.4	0.5, 0.5	
		SD, SE	2.92, 0.52	3.14, 0.99		0.19, 0.03	0.25, 0.08	
		MEDIAN	4.5	3.3		0.3	0.4	
		MIN, MAX	0.3, 13.9	0.3, 9.2		0.3, 1.3	0.3, 1.1	
		5%, 95%	0.4, 9.8	0.3, 9.2		0.3, 0.8	0.3, 1.1	
		# of BLQ/ALQ Values	1/0	1/0		31/0	3/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

PM3006439147

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 9)

Biomarker: Acetonitrile (nL/L @20 °C and 1 atm)			Analytical Lab: Madison					
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Female	Week 1	N	24	8	0.3592	23	12	0.1220
		MEAN, GEO MEAN	9197.406, 1311.823	16781.718, 3342.768		22989.985, 9938.599	38431.551, 21016.813	
		SD, SE	13705.8829, 2797.7016	19269.0303, 6812.6310		19137.6796, 3990.4821	27084.6769, 7818.6727	
		MEDIAN	439.902	7976.816		25182.623	37326.402	
		MIN, MAX	27.047, 59118.236	360.626, 43336.359		67.737, 54497.370	117.403, 90418.051	
		5%, 95%	27.047, 22265.091	360.626, 43336.359		671.507, 51712.349	117.403, 90418.051	
		# of BLQ/ALQ Values	3/8	0/4		0/0	0/0	
	Week 3	N	24	5	0.8064	28	7	0.3753
		MEAN, GEO MEAN	10294.955, 2054.833	8400.828, 1671.098		27303.463, 20657.012	36892.985, 33259.160	
		SD, SE	13820.7579, 2821.1504	13842.1107, 6190.3801		14080.9775, 2661.0546	18550.9475, 7011.5991	
		MEDIAN	722.772	360.626		28995.329	31028.322	
		MIN, MAX	27.047, 49646.042	360.626, 32326.622		703.834, 51460.152	17025.081, 64440.436	
		5%, 95%	360.626, 32770.330	360.626, 32326.622		2753.207, 44229.194	17025.081, 64440.436	
		# of BLQ/ALQ Values	1/11	0/3		0/0	0/0	
	Week 6	N	22	6	0.5795	30	5	1.0000
		MEAN, GEO MEAN	9807.737, 2250.643	10016.216, 1000.994		26894.960, 20724.486	27731.250, 26969.413	
		SD, SE	12195.4292, 2600.0742	16074.6976, 6562.4678		13112.2031, 2393.9498	7200.1256, 3219.9940	
		MEDIAN	2276.319	360.626		29198.741	29717.322	
		MIN, MAX	27.047, 37095.541	27.047, 38261.231		285.948, 58955.534	20243.545, 37028.299	
		5%, 95%	360.626, 32905.616	27.047, 38261.231		3549.774, 42384.015	20243.545, 37028.299	
		# of BLQ/ALQ Values	1/9	1/3		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 5 of 9)

Biomarker: Acetonitrile (nL/L, @20 °C and 1 atm)			Analytical Lab: Madison					
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Male	Week 1	N	10	8	0.7558	20	10	0.8603
		MEAN, GEO MEAN	16904.230, 8326.873	14316.314, 6254.584		17097.365, 7162.784	16468.872, 6236.335	
		SD, SE	20277.1984, 6412.2131	14995.5085, 5301.7129		15793.3208, 3531.4939	16455.2281, 5203.6000	
		MEDIAN	8240.636	9172.766		12584.867	8762.168	
		MIN, MAX	1283.024, 61266.718	278.352, 38265.077		27.047, 48597.939	27.047, 49048.904	
		5%, 95%	1283.024, 61266.718	278.352, 38265.077		59.975, 47313.460	27.047, 49048.904	
		# of BLQ/ALQ Values	0/0	0/0		1/0	1/0	
	Week 3	N	13	4	0.0793	23	7	0.5238
		MEAN, GEO MEAN	26388.561, 16738.102	11478.097, 9917.405		19812.928, 11507.278	25819.812, 9693.183	
		SD, SE	15238.0199, 4226.2663	6763.4827, 3381.7413		13098.5933, 2731.2455	18759.8474, 7090.5558	
		MEDIAN	29314.866	10610.769		19087.935	22947.667	
		MIN, MAX	149.199, 55212.198	4330.705, 20360.146		189.826, 41703.996	27.047, 48358.890	
		5%, 95%	149.199, 55212.198	4330.705, 20360.146		555.984, 37842.197	27.047, 48358.890	
		# of BLQ/ALQ Values	0/0	0/0		0/0	1/0	
	Week 6	N	10	4	1.0000	24	6	0.6974
		MEAN, GEO MEAN	19910.429, 13629.841	22844.579, 10705.685		24644.697, 16418.958	21592.468, 8033.725	
		SD, SE	16156.1257, 5109.0155	23809.0191, 11904.5095		14596.3978, 2979.4772	20263.5199, 8272.5473	
		MEDIAN	18654.588	19767.097		26642.053	19428.599	
		MIN, MAX	1827.506, 57117.622	2668.716, 49175.407		143.554, 47862.018	178.106, 49916.584	
		5%, 95%	1827.506, 57117.622	2668.716, 49175.407		2225.726, 46880.251	178.106, 49916.584	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

PM3006439149

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 6 of 9)

Biomarker: Acetonitrile (nL/L @20 °C and 1 atm)			Analytical Lab: Madison					
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Overall	Week 1	N	34	16	0.4829	43	22	0.2386
		MEAN, GEO MEAN	11464.119, 2259.103	15549.016, 4572.485		20249.232, 8534.252	28448.515, 12098.504	
		SD, SE	15992.7265, 2742.7300	16728.0971, 4182.0243		17706.6862, 2700.2443	25011.8052, 5332.5348	
		MEDIAN	2817.108	9172.766		16827.867	27302.458	
		MIN, MAX	27.047, 61266.718	278.352, 43336.359		27.047, 54497.370	27.047, 90418.051	
		5%, 95%	27.047, 59118.236	278.352, 43336.359		92.902, 50115.663	117.403, 74719.187	
		# of BLQ/ALQ Values	3/8	0/4		1/0	1/0	
	Week 3	N	37	9	0.5092	51	14	0.2539
		MEAN, GEO MEAN	15949.465, 4293.712	9768.503, 3687.513		23925.378, 15866.301	31356.399, 17955.142	
		SD, SE	16127.7100, 2651.3792	10751.1263, 3583.7088		14026.0527, 1964.0402	18822.1847, 5030.4405	
		MEDIAN	14371.511	8595.639		25973.434	28028.074	
		MIN, MAX	27.047, 55212.198	360.626, 32326.622		189.826, 51460.152	27.047, 64440.436	
		5%, 95%	149.199, 49646.042	360.626, 32326.622		571.554, 43507.242	27.047, 64440.436	
		# of BLQ/ALQ Values	1/11	0/3		0/0	1/0	
	Week 6	N	32	10	0.9405	54	11	0.7068
		MEAN, GEO MEAN	12964.828, 3951.292	15147.561, 2582.882		25894.843, 18686.737	24382.823, 13931.158	
		SD, SE	14112.6511, 2494.7878	19400.8827, 6135.0978		13704.2502, 1864.9122	15372.6860, 4635.0392	
		MEDIAN	8205.296	2693.761		28847.657	28310.649	
		MIN, MAX	27.047, 57117.622	27.047, 49175.407		143.554, 58955.534	178.106, 49916.584	
		5%, 95%	360.626, 37095.541	27.047, 49175.407		2225.726, 46880.251	178.106, 49916.584	
		# of BLQ/ALQ Values	1/9	1/3		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

PM3006439150

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 7 of 9)

Biomarker: Carbon monoxide (ppm)		Analytical Lab: CRF						
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value ^a	AM	PM	P-value ^a
Female	Week 1	N	23	9	0.6751	23	12	0.2026
		MEAN, GEO MEAN	25.3, 21.9	29.5, 24.7		5.2, 5.1	6.0, 5.8	
		SD, SE	13.98, 2.92	17.31, 5.77		1.14, 0.24	1.61, 0.46	
		MEDIAN	22.8	27.2		4.8	5.7	
		MIN, MAX	7.8, 66.5	8.4, 54.7		3.7, 8.1	4.0, 9.6	
		5%, 95%	9.6, 42.2	8.4, 54.7		4.0, 6.9	4.0, 9.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 2	N	22	9	0.3723	27	8	0.5818
		MEAN, GEO MEAN	27.2, 22.4	20.8, 17.2		4.4, 4.3	4.5, 4.2	
		SD, SE	18.64, 3.97	13.86, 4.62		0.99, 0.19	2.06, 0.73	
		MEDIAN	23.0	18.0		4.4	3.8	
		MIN, MAX	6.5, 88.9	6.7, 50.1		2.2, 6.8	2.1, 8.6	
		5%, 95%	9.3, 55.6	6.7, 50.1		3.2, 5.7	2.1, 8.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 3	N	24	5	0.0885	29	6	0.4433
		MEAN, GEO MEAN	28.3, 25.2	17.1, 14.1		4.6, 4.2	4.2, 4.1	
		SD, SE	12.86, 2.63	12.46, 5.57		1.41, 0.26	0.91, 0.37	
		MEDIAN	25.4	16.0		4.5	4.1	
		MIN, MAX	5.3, 60.7	7.2, 38.0		0.3, 7.4	3.0, 5.5	
		5%, 95%	12.4, 45.1	7.2, 38.0		3.1, 6.9	3.0, 5.5	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 6	N	22	6	0.5566	30	5	0.7057
		MEAN, GEO MEAN	30.1, 27.9	26.9, 19.4		5.2, 4.5	5.4, 5.4	
		SD, SE	11.15, 2.38	20.87, 8.52		2.14, 0.39	0.79, 0.35	
		MEDIAN	28.6	19.5		4.9	5.5	
		MIN, MAX	10.1, 49.9	4.0, 54.0		0.4, 9.8	4.5, 6.5	
		5%, 95%	13.6, 47.9	4.0, 54.0		1.0, 9.0	4.5, 6.5	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

^a P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 9)

Biomarker: Carbon monoxide (ppm)		Analytical Lab: CRF						
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value*	AM	PM	P-value*
Male	Week 1	N	11	7	0.9278	22	8	0.4524
		MEAN, GEO MEAN	27.0, 22.8	24.2, 21.8		6.1, 6.0	5.5, 5.3	
		SD, SE	17.63, 5.32	12.34, 4.67		1.29, 0.28	1.45, 0.51	
		MEDIAN	24.2	22.0		6.0	5.9	
		MIN, MAX	8.6, 71.4	11.6, 47.2		3.7, 9.1	3.6, 7.5	
		5%, 95%	8.6, 71.4	11.6, 47.2		4.5, 8.0	3.6, 7.5	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 2	N	13	5	0.4301	24	6	0.2871
		MEAN, GEO MEAN	24.3, 20.4	19.5, 17.6		5.6, 4.9	6.9, 6.7	
		SD, SE	12.87, 3.57	9.48, 4.24		1.47, 0.30	1.97, 0.80	
		MEDIAN	21.8	16.6		5.9	6.6	
		MIN, MAX	4.5, 44.1	9.6, 32.0		0.1, 7.7	4.8, 9.6	
		5%, 95%	4.5, 44.1	9.6, 32.0		4.0, 7.5	4.8, 9.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 3	N	14	3	0.9498	23	7	0.4029
		MEAN, GEO MEAN	25.4, 21.2	30.5, 22.9		6.1, 5.9	6.1, 6.1	
		SD, SE	14.94, 3.99	27.83, 16.07		1.78, 0.37	0.33, 0.12	
		MEDIAN	23.7	19.2		5.5	6.0	
		MIN, MAX	5.3, 55.1	10.1, 62.2		3.4, 10.6	5.8, 6.8	
		5%, 95%	5.3, 55.1	10.1, 62.2		4.0, 9.4	5.8, 6.8	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 6	N	11	3	0.7555	25	5	0.6556
		MEAN, GEO MEAN	30.1, 24.9	24.0, 19.5		7.4, 7.0	7.1, 7.0	
		SD, SE	17.49, 5.27	19.50, 11.26		2.66, 0.53	0.94, 0.42	
		MEDIAN	26.1	14.4		6.5	7.0	
		MIN, MAX	5.0, 70.5	11.1, 46.4		4.5, 13.8	6.0, 8.6	
		5%, 95%	5.0, 70.5	11.1, 46.4		4.8, 13.3	6.0, 8.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

* P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.1-4
Statistical Comparison Between AM and PM for Smokers and Non-Smokers of Selected Biomarkers of Exposure by Timepoint and Overall
(Page 9 of 9)

Biomarker: Carbon monoxide (ppm)		Analytical Lab: CRF						
Gender	Timepoint	Statistic	Smokers			Non-Smokers		
			AM	PM	P-value*	AM	PM	P-value*
Overall	Week 1	N	34	16	0.7948	45	20	0.8086
		MEAN, GEO MEAN	25.9, 22.2	27.2, 23.4		5.6, 5.5	5.8, 5.6	
		SD, SE	15.01, 2.57	15.10, 3.78		1.29, 0.19	1.52, 0.34	
		MEDIAN	23.5	23.6		5.7	5.7	
		MIN, MAX	7.8, 71.4	8.4, 54.7		3.7, 9.1	3.6, 9.6	
		5%, 95%	8.6, 66.5	8.4, 54.7		4.0, 8.0	3.7, 8.9	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 2	N	35	14	0.2590	51	14	0.6897
		MEAN, GEO MEAN	26.2, 21.6	20.3, 17.3		5.0, 4.6	5.6, 5.1	
		SD, SE	16.58, 2.80	12.10, 3.23		1.35, 0.19	2.29, 0.61	
		MEDIAN	21.8	17.3		5.0	5.3	
		MIN, MAX	4.5, 88.9	6.7, 50.1		0.1, 7.7	2.1, 9.6	
		5%, 95%	6.5, 55.6	6.7, 50.1		3.2, 7.0	2.1, 9.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 3	N	38	8	0.1778	52	13	0.6935
		MEAN, GEO MEAN	27.2, 23.7	22.1, 16.9		5.3, 4.9	5.2, 5.1	
		SD, SE	13.53, 2.20	18.93, 6.69		1.75, 0.24	1.20, 0.33	
		MEDIAN	25.0	16.2		5.1	5.8	
		MIN, MAX	5.3, 60.7	7.2, 62.2		0.3, 10.6	3.0, 6.8	
		5%, 95%	5.3, 55.1	7.2, 62.2		3.2, 8.6	3.0, 6.8	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
	Week 6	N	33	9	0.3658	55	10	0.5789
		MEAN, GEO MEAN	30.1, 26.8	25.9, 19.4		6.2, 5.5	6.2, 6.1	
		SD, SE	13.31, 2.32	19.22, 6.41		2.61, 0.35	1.21, 0.38	
		MEDIAN	28.0	14.8		5.7	6.3	
		MIN, MAX	5.0, 70.5	4.0, 54.0		0.4, 13.8	4.5, 8.6	
		5%, 95%	10.0, 49.9	4.0, 54.0		1.3, 11.6	4.5, 8.6	
		# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

NOTE: AM refers to biomarker collection before noon, PM refers to biomarker collection at noon or after.

* P-value from Wilcoxon rank-sum test.

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Protocol No. PM-8450

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14.2.2 Comparison Between Smokers and Non-Smokers by Gender

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 14)

Biomarker: Acetonitrile (ng/mL)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	0.0003	32	35	0.0001
	MEAN, GEO MEAN	477.23, 333.46	171.70, 106.37		221.90, 173.46	184.61, 90.50	
	SD, SE	377.102, 88.884	258.462, 47.189		248.932, 44.005	313.664, 53.019	
	MEDIAN	312.53	107.85		154.60	88.39	
	MIN, MAX	51.48, 1346.61	30.00, 1436.84		66.48, 1500.00	30.00, 1500.00	
	5%, 95%	51.48, 1346.61	30.00, 431.13		75.16, 386.20	30.00, 972.68	
	# of BLQ/ALQ Values	1/0	8/0		0/1	8/1	
Week 2	N	17	30	0.0010	31	35	0.0154
	MEAN, GEO MEAN	436.61, 318.33	164.07, 114.31		314.55, 212.48	192.29, 116.73	
	SD, SE	360.287, 87.383	143.259, 26.155		313.375, 56.284	201.926, 34.132	
	MEDIAN	285.73	112.33		179.28	95.44	
	MIN, MAX	54.06, 1500.00	30.00, 688.37		30.00, 1500.00	30.00, 756.74	
	5%, 95%	54.06, 1500.00	30.00, 371.86		48.66, 1002.96	30.00, 664.01	
	# of BLQ/ALQ Values	0/1	7/0		1/1	5/0	
Week 3	N	17	30	0.0001	29	35	0.0014
	MEAN, GEO MEAN	820.39, 583.11	234.01, 153.58		383.39, 251.66	182.84, 118.86	
	SD, SE	694.688, 168.487	216.278, 39.487		429.385, 79.735	221.687, 37.472	
	MEDIAN	429.35	150.45		239.93	109.58	
	MIN, MAX	166.78, 2000.00	30.00, 896.92		46.59, 2000.00	30.00, 1168.91	
	5%, 95%	166.78, 2000.00	30.00, 722.48		67.97, 1389.35	30.00, 619.94	
	# of BLQ/ALQ Values	0/4	6/0		0/1	4/0	
Week 6	N	14	30	0.0012	28	35	0.0731
	MEAN, GEO MEAN	477.27, 375.66	203.58, 125.40		420.84, 251.72	242.70, 141.68	
	SD, SE	261.951, 70.009	224.030, 40.902		485.955, 91.837	241.581, 40.835	
	MEDIAN	509.88	108.47		173.79	150.96	
	MIN, MAX	31.68, 1060.80	30.00, 886.61		49.12, 1500.00	30.00, 947.36	
	5%, 95%	31.68, 1060.80	30.00, 744.35		97.44, 1460.56	30.00, 670.92	
	# of BLQ/ALQ Values	0/0	6/0		0/1	7/0	
Overall ^b	N	18	30	<.0001	32	35	0.0127
	MEAN, GEO MEAN	556.01, 495.30	193.34, 167.20		326.87, 258.33	200.61, 153.31	
	SD, SE	278.491, 65.641	105.774, 19.312		230.694, 40.781	157.950, 26.699	
	MEDIAN	472.90	153.90		253.44	156.31	
	MIN, MAX	204.49, 1084.24	41.94, 452.36		82.80, 951.72	30.00, 701.92	
	5%, 95%	204.49, 1084.24	83.94, 382.94		85.41, 740.98	40.12, 599.86	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 14)

Biomarker: Acetonitrile (nmol/L)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	0.0003	32	35	0.0001
	MEAN, GEO MEAN	11634.8, 8129.7	4186.1, 2593.3		5409.8, 4228.9	4500.7, 2206.4	
	SD, SE	9193.74, 2166.99	6301.32, 1150.46		6068.97, 1072.85	7647.13, 1292.60	
	MEDIAN	7619.5	2629.3		3769.2	2154.9	
	MIN, MAX	1255.1, 32830.4	731.4, 35030.2		1620.8, 36570.0	731.4, 36570.0	
	5%, 95%	1255.1, 32830.4	731.4, 10510.9		1832.4, 9415.6	731.4, 23713.9	
	# of BLQ/ALQ Values	1/0	8/0		0/1	8/1	
Week 2	N	17	30	0.0010	31	35	0.0154
	MEAN, GEO MEAN	10644.6, 7760.9	3999.9, 2786.9		7668.8, 5180.2	4688.1, 2845.8	
	SD, SE	8783.81, 2130.39	3492.67, 637.67		7640.09, 1372.20	4922.96, 832.13	
	MEDIAN	6966.1	2738.5		4370.8	2326.8	
	MIN, MAX	1318.0, 36570.0	731.4, 16782.5		731.4, 36570.0	731.4, 18449.3	
	5%, 95%	1318.0, 36570.0	731.4, 9065.9		1186.3, 24452.2	731.4, 16188.6	
	# of BLQ/ALQ Values	0/1	7/0		1/1	5/0	
Week 3	N	17	30	0.0001	29	35	0.0014
	MEAN, GEO MEAN	20001.2, 14216.3	5705.1, 3744.2		9347.0, 6135.5	4457.7, 2897.8	
	SD, SE	16936.49, 4107.70	5272.86, 962.69		10468.41, 1943.94	5404.72, 913.56	
	MEDIAN	10467.6	3668.0		5849.5	2671.6	
	MIN, MAX	4066.1, 48760.0	731.4, 21866.9		1135.9, 48760.0	731.4, 28498.0	
	5%, 95%	4066.1, 48760.0	731.4, 17614.1		1657.1, 33872.4	731.4, 15114.1	
	# of BLQ/ALQ Values	0/4	6/0		0/1	4/0	
Week 6	N	14	30	0.0012	28	35	0.0731
	MEAN, GEO MEAN	11635.7, 9158.6	4963.4, 3057.3		10260.1, 6136.8	5917.0, 3454.2	
	SD, SE	6386.36, 1706.83	5461.86, 997.20		11847.57, 2238.98	5889.73, 995.55	
	MEDIAN	12430.9	2644.5		4237.0	3680.4	
	MIN, MAX	772.4, 25862.3	731.4, 21615.6		1197.5, 36570.0	731.4, 23096.6	
	5%, 95%	772.4, 25862.3	731.4, 18147.3		2375.6, 35608.5	731.4, 16357.0	
	# of BLQ/ALQ Values	0/0	6/0		0/1	7/0	
Overall ^b	N	18	30	<.0001	32	35	0.0127
	MEAN, GEO MEAN	13555.4, 12075.3	4713.6, 4076.3		7969.0, 6298.0	4890.9, 3737.6	
	SD, SE	6789.62, 1600.33	2578.76, 470.82		5624.31, 994.25	3850.84, 650.91	
	MEDIAN	11529.4	3752.0		6178.8	3810.7	
	MIN, MAX	4985.5, 26433.8	1022.5, 11028.6		2018.6, 23202.8	731.4, 17112.8	
	5%, 95%	4985.5, 26433.8	2046.5, 9336.2		2082.3, 18065.1	978.1, 14624.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 14)

Biomarker: Acetonitrile ((ng/mL)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	38.45, 26.28			17.29, 13.14		
	SD, SE	31.993, 7.541			16.633, 2.940		
	MEDIAN	33.25			11.57		
	MIN, MAX	5.47, 116.91			3.39, 88.24		
	5%, 95%	5.47, 116.91			4.18, 53.45		
	# of BLQ/ALQ Values	1/0			0/1		
Week 2	N	17		NA	31		NA
	MEAN, GEO MEAN	40.21, 23.17			27.93, 17.33		
	SD, SE	54.195, 13.144			34.908, 6.270		
	MEDIAN	25.98			13.65		
	MIN, MAX	6.76, 205.14			3.93, 174.28		
	5%, 95%	6.76, 205.14			4.11, 100.00		
	# of BLQ/ALQ Values	0/1			1/1		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	103.43, 54.84			29.62, 18.21		
	SD, SE	112.492, 27.283			35.787, 6.646		
	MEDIAN	35.03			14.37		
	MIN, MAX	9.05, 333.33			4.25, 158.87		
	5%, 95%	9.05, 333.33			4.89, 100.00		
	# of BLQ/ALQ Values	0/4			0/1		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	41.76, 29.28			50.12, 18.48		
	SD, SE	38.051, 10.170			131.352, 24.823		
	MEDIAN	31.82			14.19		
	MIN, MAX	3.17, 149.45			4.87, 703.19		
	5%, 95%	3.17, 149.45			5.17, 127.61		
	# of BLQ/ALQ Values	0/0			0/1		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	56.35, 42.29			30.71, 20.49		
	SD, SE	43.360, 10.220			44.995, 7.954		
	MEDIAN	40.20			22.09		
	MIN, MAX	8.68, 143.31			4.35, 264.63		
	5%, 95%	8.68, 143.31			7.10, 55.99		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Acetonitrile ((nmol/L)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	937.3, 640.7			421.5, 320.2		
	SD, SE	779.97, 183.84			405.51, 71.68		
	MEDIAN	810.6			282.1		
	MIN, MAX	133.3, 2850.2			82.7, 2151.2		
	5%, 95%	133.3, 2850.2			101.8, 1303.1		
	# of BLQ/ALQ Values	1/0			0/1		
Week 2	N	17		NA	31		NA
	MEAN, GEO MEAN	980.3, 564.9			681.0, 422.5		
	SD, SE	1321.27, 320.46			851.05, 152.85		
	MEDIAN	633.3			332.9		
	MIN, MAX	164.7, 5001.3			95.9, 4249.0		
	5%, 95%	164.7, 5001.3			100.1, 2438.0		
	# of BLQ/ALQ Values	0/1			1/1		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2521.5, 1337.1			722.2, 443.9		
	SD, SE	2742.59, 665.18			872.48, 162.02		
	MEDIAN	854.1			350.4		
	MIN, MAX	220.7, 8126.7			103.6, 3873.2		
	5%, 95%	220.7, 8126.7			119.3, 2438.0		
	# of BLQ/ALQ Values	0/4			0/1		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	1018.0, 713.8			1221.9, 450.4		
	SD, SE	927.67, 247.93			3202.36, 605.19		
	MEDIAN	775.9			345.9		
	MIN, MAX	77.2, 3643.5			118.8, 17143.8		
	5%, 95%	77.2, 3643.5			126.1, 3111.1		
	# of BLQ/ALQ Values	0/0			0/1		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	1373.8, 1031.0			748.7, 499.4		
	SD, SE	1057.14, 249.17			1096.97, 193.92		
	MEDIAN	980.1			538.5		
	MIN, MAX	211.5, 3493.7			106.1, 6451.6		
	5%, 95%	211.5, 3493.7			173.0, 1364.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 5 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: Harrogate

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	4.79, 3.24	0.51, 0.50		3.22, 2.43	0.67, 0.57	
	SD, SE	4.325, 1.019	0.022, 0.004		2.592, 0.466	0.692, 0.117	
	MEDIAN	2.88	0.50		2.03	0.50	
	MIN, MAX	0.50, 15.03	0.50, 0.62		0.50, 10.41	0.50, 4.59	
	5%, 95%	0.50, 15.03	0.50, 0.53		0.95, 9.39	0.50, 0.97	
	# of BLQ/ALQ Values	1/0	27/0		1/0	26/0	
Week 6	N	14	30	<.0001	28	35	<.0001
	MEAN, GEO MEAN	4.70, 3.32	0.59, 0.55		5.70, 2.76	0.59, 0.56	
	SD, SE	3.885, 1.038	0.385, 0.070		11.736, 2.218	0.292, 0.049	
	MEDIAN	3.15	0.50		2.70	0.50	
	MIN, MAX	0.50, 12.65	0.50, 2.46		0.50, 63.34	0.50, 1.84	
	5%, 95%	0.50, 12.65	0.50, 1.35		0.50, 13.54	0.50, 1.45	
	# of BLQ/ALQ Values	1/0	28/0		2/0	31/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4.62, 3.23	0.55, 0.53		4.26, 2.71	0.63, 0.58	
	SD, SE	3.929, 0.926	0.197, 0.036		5.775, 1.021	0.370, 0.063	
	MEDIAN	2.97	0.50		2.36	0.50	
	MIN, MAX	0.50, 13.35	0.50, 1.48		0.50, 32.18	0.50, 2.55	
	5%, 95%	0.50, 13.35	0.50, 0.99		0.81, 11.98	0.50, 1.17	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 6 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct ((pg/g hemoglobin/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	0.35, 0.25			0.23, 0.19		
	SD, SE	0.310, 0.073			0.146, 0.026		
	MEDIAN	0.24			0.17		
	MIN, MAX	0.08, 1.17			0.06, 0.57		
	5%, 95%	0.08, 1.17			0.06, 0.47		
	# of BLQ/ALQ Values	1/0			1/0		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	0.46, 0.26			1.35, 0.20		
	SD, SE	0.670, 0.179			5.945, 1.124		
	MEDIAN	0.21			0.17		
	MIN, MAX	0.06, 2.60			0.03, 31.67		
	5%, 95%	0.06, 2.60			0.05, 0.66		
	# of BLQ/ALQ Values	1/0			2/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	0.38, 0.26			0.73, 0.22		
	SD, SE	0.434, 0.102			2.793, 0.494		
	MEDIAN	0.23			0.22		
	MIN, MAX	0.07, 1.82			0.05, 16.01		
	5%, 95%	0.07, 1.82			0.06, 0.57		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 7 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	45.39, 37.62	6.28, 5.66		28.01, 24.04	8.13, 7.35	
	SD, SE	27.734, 6.537	3.023, 0.552		14.440, 2.594	4.064, 0.687	
	MEDIAN	38.12	5.39		25.56	6.80	
	MIN, MAX	12.37, 100.50	2.90, 13.87		5.35, 67.83	2.49, 23.25	
	5%, 95%	12.37, 100.50	3.12, 13.59		5.37, 50.52	2.95, 17.37	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 6	N	14	30	<.0001	28	35	<.0001
	MEAN, GEO MEAN	44.70, 37.31	8.92, 7.86		66.16, 38.07	8.71, 8.05	
	SD, SE	25.972, 6.941	5.287, 0.965		146.613, 27.707	3.907, 0.660	
	MEDIAN	41.52	7.43		37.63	7.53	
	MIN, MAX	9.56, 97.75	4.11, 27.86		7.27, 808.80	4.09, 22.67	
	5%, 95%	9.56, 97.75	4.31, 20.64		7.32, 90.32	4.36, 15.91	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	43.73, 36.74	7.60, 6.81		44.63, 31.28	8.43, 7.84	
	SD, SE	25.307, 5.965	3.989, 0.728		68.194, 12.055	3.697, 0.625	
	MEDIAN	41.27	6.49		32.62	7.17	
	MIN, MAX	12.37, 99.13	3.62, 20.87		6.31, 408.68	4.07, 22.96	
	5%, 95%	12.37, 99.13	3.83, 15.04		6.35, 79.08	4.71, 16.35	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (ng/g hemoglobin/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	3.96, 2.96			2.12, 1.84		
	SD, SE	3.964, 0.934			1.247, 0.224		
	MEDIAN	2.86			1.75		
	MIN, MAX	0.71, 18.14			0.59, 6.43		
	5%, 95%	0.71, 18.14			0.90, 4.79		
	# of BLQ/ALQ Values	0/0			0/0		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	5.19, 2.91			16.89, 2.79		
	SD, SE	9.231, 2.467			75.953, 14.354		
	MEDIAN	2.07			2.43		
	MIN, MAX	1.08, 36.66			0.95, 404.40		
	5%, 95%	1.08, 36.66			1.29, 6.49		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	4.26, 2.92			8.66, 2.46		
	SD, SE	5.997, 1.414			35.599, 6.293		
	MEDIAN	2.63			1.97		
	MIN, MAX	0.90, 27.40			0.93, 203.63		
	5%, 95%	0.90, 27.40			1.16, 6.43		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 9 of 14)

Biomarker: Carboxyhemoglobin (% saturation) Analytical Lab: CCLS

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4.4, 3.3	0.5, 0.4		4.5, 3.4	0.3, 0.3	
	SD, SE	3.35, 0.79	0.20, 0.04		3.07, 0.54	0.08, 0.01	
	MEDIAN	4.0	0.4		3.8	0.3	
	MIN, MAX	0.3, 14.8	0.3, 1.0		0.8, 11.4	0.3, 0.7	
	5%, 95%	0.3, 14.8	0.3, 0.8		0.9, 11.3	0.3, 0.5	
	# of BLQ/ALQ Values	1/0	12/0		0/0	27/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	3.7, 2.7	0.4, 0.4		4.2, 2.8	0.3, 0.3	
	SD, SE	2.69, 0.63	0.22, 0.04		3.21, 0.58	0.05, 0.01	
	MEDIAN	3.0	0.3		3.7	0.3	
	MIN, MAX	0.3, 8.6	0.3, 1.1		0.3, 13.3	0.3, 0.5	
	5%, 95%	0.3, 8.6	0.3, 0.9		0.3, 10.1	0.3, 0.5	
	# of BLQ/ALQ Values	1/0	17/0		2/0	30/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	4.7, 3.4	0.5, 0.4		4.8, 3.8	0.5, 0.4	
	SD, SE	3.52, 0.85	0.47, 0.09		2.78, 0.52	0.53, 0.09	
	MEDIAN	3.8	0.3		4.1	0.3	
	MIN, MAX	0.3, 11.3	0.3, 2.8		0.3, 9.7	0.3, 2.5	
	5%, 95%	0.3, 11.3	0.3, 1.0		0.7, 9.3	0.3, 2.2	
	# of BLQ/ALQ Values	1/0	16/0		0/0	22/0	
Week 6	N	13	30	<.0001	28	35	<.0001
	MEAN, GEO MEAN	4.9, 3.5	0.4, 0.4		4.6, 3.5	0.4, 0.4	
	SD, SE	3.55, 0.99	0.20, 0.04		2.72, 0.51	0.21, 0.03	
	MEDIAN	4.1	0.3		4.3	0.3	
	MIN, MAX	0.3, 13.9	0.3, 1.1		0.3, 9.8	0.3, 1.3	
	5%, 95%	0.3, 13.9	0.3, 0.9		0.4, 9.2	0.3, 0.8	
	# of BLQ/ALQ Values	1/0	12/0		1/0	22/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4.2, 3.2	0.5, 0.4		4.4, 3.4	0.4, 0.4	
	SD, SE	3.00, 0.71	0.20, 0.04		2.89, 0.51	0.17, 0.03	
	MEDIAN	3.6	0.4		4.1	0.3	
	MIN, MAX	0.3, 12.2	0.3, 1.3		0.6, 11.0	0.3, 1.1	
	5%, 95%	0.3, 12.2	0.3, 0.8		0.7, 9.8	0.3, 0.9	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 10 of 14)

Biomarker: Carboxyhemoglobin ((% saturation)/cigarette per day)		Analytical Lab: CCLS			
Timepoint	Statistic	Male		P-value*	
		Smokers	Non-Smokers		
Week 1	N	18		NA	32
	MEAN, GEO MEAN	0.4, 0.3			0.3, 0.3
	SD, SE	0.67, 0.16			0.18, 0.03
	MEDIAN	0.2			0.3
	MIN, MAX	0.1, 3.0			0.1, 0.8
	5%, 95%	0.1, 3.0			0.1, 0.8
	# of BLQ/ALQ Values	1/0			0/0
Week 2	N	18		NA	31
	MEAN, GEO MEAN	0.4, 0.2			0.3, NA
	SD, SE	0.97, 0.23			0.19, 0.03
	MEDIAN	0.2			0.2
	MIN, MAX	0.1, 4.3			0.0, 1.0
	5%, 95%	0.1, 4.3			0.1, 0.5
	# of BLQ/ALQ Values	1/0			2/0
Week 3	N	17		NA	29
	MEAN, GEO MEAN	0.5, 0.3			0.3, 0.3
	SD, SE	0.51, 0.12			0.20, 0.04
	MEDIAN	0.3			0.3
	MIN, MAX	0.1, 2.3			0.1, 1.1
	5%, 95%	0.1, 2.3			0.1, 0.6
	# of BLQ/ALQ Values	1/0			0/0
Week 6	N	13		NA	28
	MEAN, GEO MEAN	0.8, 0.3			0.3, 0.3
	SD, SE	1.88, 0.52			0.23, 0.04
	MEDIAN	0.2			0.3
	MIN, MAX	0.1, 7.0			0.1, 1.3
	5%, 95%	0.1, 7.0			0.1, 0.7
	# of BLQ/ALQ Values	1/0			1/0
Overall*	N	18		NA	32
	MEAN, GEO MEAN	0.5, 0.3			0.3, 0.3
	SD, SE	0.93, 0.22			0.19, 0.03
	MEDIAN	0.3			0.3
	MIN, MAX	0.1, 4.2			0.1, 1.1
	5%, 95%	0.1, 4.2			0.1, 0.7

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 11 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: INBIFO

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	2	4	0.7237	1	4	NA
	MEAN, GEO MEAN	0.70, 0.70	2.17, 1.23		0.70, 0.70	0.70, 0.70	
	SD, SE	0.000, 0.000	2.945, 1.473		NA, NA	0.000, 0.000	
	MEDIAN	0.70	0.70		0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 6.59		0.70, 0.70	0.70, 0.70	
	5%, 95%	0.70, 0.70	0.70, 6.59		NA, NA	0.70, 0.70	
	# of BLQ/ALQ Values	2/0	3/0		1/0	4/0	
Week 6	N	2	4	1.0000	1	4	NA
	MEAN, GEO MEAN	0.70, 0.70	0.70, 0.70		0.70, 0.70	0.70, 0.70	
	SD, SE	0.000, 0.000	0.000, 0.000		NA, NA	0.000, 0.000	
	MEDIAN	0.70	0.70		0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 0.70		0.70, 0.70	0.70, 0.70	
	5%, 95%	0.70, 0.70	0.70, 0.70		NA, NA	0.70, 0.70	
	# of BLQ/ALQ Values	2/0	4/0		1/0	4/0	
Overall ^b	N	3	4	0.5637	2	4	1.0000
	MEAN, GEO MEAN	0.70, 0.70	1.44, 1.06		0.70, 0.70	0.70, 0.70	
	SD, SE	0.000, 0.000	1.475, 0.738		0.000, 0.000	0.000, 0.000	
	MEDIAN	0.70	0.70		0.70	0.70	
	MIN, MAX	0.70, 0.70	0.70, 3.65		0.70, 0.70	0.70, 0.70	
	5%, 95%	0.70, 0.70	0.70, 3.65		0.70, 0.70	0.70, 0.70	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 12 of 14)

Biomarker: 3-Aminobiphenyl-Hb adduct (pg/g hemoglobin/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	2		NA	1		NA
	MEAN, GEO MEAN	0.08, 0.07			0.06, 0.06		
	SD, SE	0.057, 0.040			NA, NA		
	MEDIAN	0.08			0.06		
	MIN, MAX	0.04, 0.12			0.06, 0.06		
	5%, 95%	0.04, 0.12			NA, NA		
	# of BLQ/ALQ Values	2/0			1/0		
Week 6	N	2		NA	1		NA
	MEAN, GEO MEAN	0.06, 0.05			0.18, 0.18		
	SD, SE	0.021, 0.015			NA, NA		
	MEDIAN	0.06			0.18		
	MIN, MAX	0.04, 0.07			0.18, 0.18		
	5%, 95%	0.04, 0.07			NA, NA		
	# of BLQ/ALQ Values	2/0			1/0		
Overall ^b	N	3		NA	2		NA
	MEAN, GEO MEAN	0.06, 0.05			0.12, 0.10		
	SD, SE	0.035, 0.020			0.085, 0.060		
	MEDIAN	0.04			0.12		
	MIN, MAX	0.04, 0.10			0.06, 0.18		
	5%, 95%	0.04, 0.10			0.06, 0.18		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 13 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct (pg/g hemoglobin) Analytical Lab: INBIFO

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	4	4	0.0304	3	4	0.0518
	MEAN, GEO MEAN	28.28, 27.74	9.64, 9.20		40.03, 37.23	11.21, 10.48	
	SD, SE	6.004, 3.002	3.405, 1.702		19.605, 11.319	4.996, 2.498	
	MEDIAN	29.75	9.06		29.87	9.68	
	MIN, MAX	19.77, 33.83	6.74, 13.71		27.59, 62.63	7.07, 18.39	
	5%, 95%	19.77, 33.83	6.74, 13.71		27.59, 62.63	7.07, 18.39	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 6	N	3	4	0.2159	4	4	0.0304
	MEAN, GEO MEAN	18.19, 18.13	13.06, 12.31		43.37, 39.47	9.54, 9.09	
	SD, SE	1.828, 1.055	4.998, 2.499		23.707, 11.853	3.683, 1.842	
	MEDIAN	17.44	12.85		33.69	8.14	
	MIN, MAX	16.85, 20.27	7.30, 19.24		27.83, 78.25	6.90, 14.99	
	5%, 95%	16.85, 20.27	7.30, 19.24		27.83, 78.25	6.90, 14.99	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	4	4	0.0304	4	4	0.0304
	MEAN, GEO MEAN	24.61, 24.24	11.35, 10.93		40.34, 39.14	10.38, 9.81	
	SD, SE	4.738, 2.369	3.433, 1.717		11.431, 5.715	4.315, 2.158	
	MEDIAN	25.46	11.54		39.06	8.91	
	MIN, MAX	18.31, 29.21	7.11, 15.22		29.19, 54.06	6.99, 16.69	
	5%, 95%	18.31, 29.21	7.11, 15.22		29.19, 54.06	6.99, 16.69	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-1
Statistical Comparison Between Smokers and Non-Smokers by Gender of Blood and/or Plasma Biomarkers of Exposure by Timepoint and Overall
(Page 14 of 14)

Biomarker: 4-Aminobiphenyl-Hb adduct ((pg/g hemoglobin)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	4		NA	3		NA
	MEAN, GEO MEAN	3.32, 2.90			6.32, 3.30		
	SD, SE	1.924, 0.962			8.115, 4.685		
	MEDIAN	2.99			2.30		
	MIN, MAX	1.68, 5.64			1.00, 15.66		
	5%, 95%	1.68, 5.64			1.00, 15.66		
	# of BLQ/ALQ Values	0/0			0/0		
Week 6	N	3		NA	4		NA
	MEAN, GEO MEAN	1.30, 1.21			3.80, 3.44		
	SD, SE	0.636, 0.367			2.134, 1.067		
	MEDIAN	0.97			2.90		
	MIN, MAX	0.89, 2.03			2.43, 6.96		
	5%, 95%	0.89, 2.03			2.43, 6.96		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	4		NA	4		NA
	MEAN, GEO MEAN	2.67, 2.32			4.57, 3.42		
	SD, SE	1.545, 0.772			4.508, 2.254		
	MEDIAN	2.60			2.59		
	MIN, MAX	1.33, 4.17			1.81, 11.31		
	5%, 95%	1.33, 4.17			1.81, 11.31		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 264)

Biomarker: NNAL (pg/24hr)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	191274.750, 138941.078	10411.800, 9179.577		281919.984, 211578.900	12534.831, 11115.607	
	SD, SE	118708.1704, 27979.7841	5411.7101, 988.0386		201340.9792, 35592.3929	6518.8212, 1101.8819	
	MEDIAN	192779.000	8190.000		234058.500	11100.000	
	MIN, MAX	8460.000, 409840.000	3180.000, 22800.000		16500.000, 852355.000	3420.000, 30796.800	
	5%, 95%	8460.000, 409840.000	3900.000, 20100.000		23940.000, 671265.000	4800.000, 27840.000	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	229255.471, 150668.308	15485.700, 12411.461		307183.903, 256566.325	12785.229, 11917.008	
	SD, SE	184405.3931, 44724.8773	12690.8350, 2317.0189		164685.2029, 30581.2745	4916.9699, 831.1196	
	MEDIAN	162848.000	11400.000		286356.000	12180.000	
	MIN, MAX	6288.000, 573980.000	4500.000, 57240.000		45936.000, 781704.000	5640.000, 28440.000	
	5%, 95%	6288.000, 573980.000	4500.000, 52910.000		52452.000, 535470.000	5940.000, 20100.000	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	210260.875, 149953.882	12948.750, 11411.289		287126.995, 234337.908	12670.040, 11705.685	
	SD, SE	140301.9013, 33069.4753	7000.2068, 1278.0570		166377.3100, 29411.6310	5321.9122, 899.5673	
	MEDIAN	185850.500	10033.500		262596.375	11790.000	
	MIN, MAX	7374.000, 426577.000	3840.000, 32310.000		34476.000, 589956.000	5910.000, 28140.000	
	5%, 95%	7374.000, 426577.000	5280.000, 29095.000		53922.000, 588892.500	6450.000, 24998.400	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 264)

Biomarker: NNAL (pmol/24hr)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	914.293, 664.139	49.768, 43.878		1347.578, 1011.347	60.012, 53.133	
	SD, SE	567.4251, 133.7434	25.8680, 4.7228		962.4099, 170.1316	31.1599, 5.2670	
	MEDIAN	921.484	39.148		1118.800	53.058	
	MIN, MAX	40.439, 1959.035	15.200, 108.984		78.870, 4074.257	16.348, 147.209	
	5%, 95%	40.439, 1959.035	18.642, 96.078		114.433, 3208.647	22.944, 133.075	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1095.841, 720.195	74.022, 59.327		1468.339, 1226.387	61.113, 56.963	
	SD, SE	881.4577, 213.7849	60.6622, 11.0754		787.1953, 146.1785	23.5031, 3.9727	
	MEDIAN	778.413	54.492		1368.782	58.220	
	MIN, MAX	30.057, 2743.624	21.510, 273.607		219.574, 3736.545	26.959, 135.943	
	5%, 95%	30.057, 2743.624	21.510, 252.910		250.721, 2559.547	28.393, 96.078	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall†	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1005.047, 716.780	61.895, 54.546		1372.467, 1120.135	60.563, 55.953	
	SD, SE	670.6430, 158.0721	33.4610, 6.1091		795.2836, 140.5876	25.4387, 4.2999	
	MEDIAN	888.366	47.961		1255.211	56.357	
	MIN, MAX	35.248, 2039.038	18.355, 154.442		164.796, 2819.990	28.250, 134.509	
	5%, 95%	35.248, 2039.038	25.239, 139.074		257.747, 2814.907	30.831, 119.493	

* P-value from Wilcoxon rank-sum test.

† Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 264)

Biomarker: NNAL (ng/24hr)/cigarette per day Analytical Lab: Madison

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	14085.758, 10948.960			20419.190, 16021.124		
	SD, SE	11496.8277, 2709.8283			16442.9829, 2906.7362		
	MEDIAN	9920.500			14300.465		
	MIN, MAX	2820.000, 50956.800			5781.000, 85235.500		
	5%, 95%	2820.000, 50956.800			5852.273, 46530.000		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	17404.532, 14171.545			21914.687, 18561.087		
	SD, SE	9655.2960, 2341.7533			14064.9755, 2611.8004		
	MEDIAN	16640.000			16884.000		
	MIN, MAX	2096.000, 36162.000			7314.000, 64500.000		
	5%, 95%	2096.000, 36162.000			7826.000, 52113.600		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	15538.380, 12750.184			21374.985, 18123.410		
	SD, SE	9552.7621, 2251.6076			13308.0772, 2352.5579		
	MEDIAN	14099.908			15865.686		
	MIN, MAX	2458.000, 41763.200			6803.500, 62355.425		
	5%, 95%	2458.000, 41763.200			6936.783, 46530.000		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 264)

Biomarker: NNAL ((pmol/24hr)/cigarette per day) Analytical Lab: Madison

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	67.330, 52.336			97.604, 76.581		
	SD, SE	54.9549, 12.9530			78.5975, 13.8942		
	MEDIAN	47.420			68.356		
	MIN, MAX	13.480, 243.574			27.633, 407.426		
	5%, 95%	13.480, 243.574			27.974, 222.413		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	83.194, 67.740			104.752, 88.722		
	SD, SE	46.1524, 11.1936			67.2306, 12.4844		
	MEDIAN	79.539			80.706		
	MIN, MAX	10.019, 172.854			34.961, 308.310		
	5%, 95%	10.019, 172.854			37.408, 249.103		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	74.274, 60.946			102.173, 86.630		
	SD, SE	45.6623, 10.7627			63.6126, 11.2452		
	MEDIAN	67.398			75.838		
	MIN, MAX	11.750, 199.629			32.521, 298.059		
	5%, 95%	11.750, 199.629			33.158, 222.413		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL (pg/mg Creatinine)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	160.048, 105.095	5.942, 5.166		252.415, 184.524	10.689, 9.434	
	SD, SE	171.2216, 40.3573	3.3379, 0.6094		181.5307, 32.0904	5.4597, 0.9229	
	MEDIAN	105.373	4.491		208.248	9.509	
	MIN, MAX	7.958, 767.052	1.932, 14.815		12.795, 813.359	2.285, 29.814	
	5%, 95%	7.958, 767.052	2.683, 11.788		13.730, 612.755	3.436, 20.782	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	153.041, 108.730	8.665, 6.794		270.188, 218.820	11.615, 10.332	
	SD, SE	106.2859, 25.7781	6.9510, 1.2691		171.0361, 31.7606	5.7724, 0.9757	
	MEDIAN	109.091	6.367		225.402	10.657	
	MIN, MAX	5.525, 368.503	2.158, 30.264		47.240, 724.324	3.259, 30.000	
	5%, 95%	5.525, 368.503	2.413, 29.578		52.222, 553.597	3.795, 23.715	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	155.884, 110.331	7.304, 6.332		260.848, 202.542	11.152, 10.111	
	SD, SE	125.4039, 29.5580	4.0261, 0.7351		177.8695, 31.4432	4.8999, 0.8282	
	MEDIAN	121.636	5.790		207.009	10.520	
	MIN, MAX	6.742, 522.399	2.364, 17.426		32.976, 768.842	3.348, 23.043	
	5%, 95%	6.742, 522.399	2.693, 16.420		34.373, 612.755	4.532, 21.741	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 6 of 264)

Biomarker: NNAL (pmol/mg Creatinine)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	0.765, 0.502	0.028, 0.025		1.207, 0.882	0.051, 0.045	
	SD, SE	0.8185, 0.1929	0.0160, 0.0029		0.8678, 0.1534	0.0262, 0.0044	
	MEDIAN	0.504	0.022		0.996	0.045	
	MIN, MAX	0.038, 3.667	0.009, 0.071		0.061, 3.888	0.011, 0.143	
	5%, 95%	0.038, 3.667	0.013, 0.056		0.066, 2.929	0.016, 0.099	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	0.731, 0.519	0.041, 0.032		1.291, 1.046	0.056, 0.049	
	SD, SE	0.5080, 0.1232	0.0332, 0.0061		0.8175, 0.1518	0.0275, 0.0046	
	MEDIAN	0.521	0.031		1.077	0.051	
	MIN, MAX	0.026, 1.761	0.010, 0.145		0.226, 3.462	0.016, 0.143	
	5%, 95%	0.026, 1.761	0.012, 0.141		0.250, 2.646	0.018, 0.113	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	0.745, 0.527	0.035, 0.030		1.247, 0.968	0.054, 0.049	
	SD, SE	0.5996, 0.1413	0.0193, 0.0035		0.8503, 0.1503	0.0233, 0.0039	
	MEDIAN	0.582	0.028		0.990	0.051	
	MIN, MAX	0.032, 2.498	0.011, 0.084		0.158, 3.675	0.016, 0.110	
	5%, 95%	0.032, 2.498	0.013, 0.079		0.164, 2.929	0.022, 0.104	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL ((pg/mg Creatinine)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	16.423, 8.282			17.616, 13.972		
	SD, SE	34.5325, 8.1394			12.0923, 2.1376		
	MEDIAN	6.962			14.081		
	MIN, MAX	2.653, 153.410			3.199, 51.694		
	5%, 95%	2.653, 153.410			4.430, 40.850		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	13.465, 10.227			19.709, 15.830		
	SD, SE	12.1015, 2.9350			15.4795, 2.8745		
	MEDIAN	12.019			13.056		
	MIN, MAX	1.842, 55.549			6.429, 69.200		
	5%, 95%	1.842, 55.549			6.641, 61.602		
	# of BLQ/ALQ Values	1/0			0/0		
Overall [*]	N	18		NA	32		NA
	MEAN, GEO MEAN	14.726, 9.379			19.095, 15.708		
	SD, SE	22.8841, 5.3938			12.7178, 2.2482		
	MEDIAN	9.583			14.886		
	MIN, MAX	2.248, 104.480			5.430, 60.447		
	5%, 95%	2.248, 104.480			5.699, 40.850		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.079, 0.040			0.084, 0.067		
	SD, SE	0.1650, 0.0389			0.0578, 0.0102		
	MEDIAN	0.034			0.067		
	MIN, MAX	0.013, 0.733			0.015, 0.247		
	5%, 95%	0.013, 0.733			0.021, 0.195		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.064, 0.049			0.094, 0.076		
	SD, SE	0.0580, 0.0141			0.0740, 0.0137		
	MEDIAN	0.057			0.063		
	MIN, MAX	0.009, 0.266			0.031, 0.331		
	5%, 95%	0.009, 0.266			0.032, 0.295		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.071, 0.045			0.092, 0.076		
	SD, SE	0.1095, 0.0258			0.0608, 0.0107		
	MEDIAN	0.046			0.072		
	MIN, MAX	0.011, 0.500			0.026, 0.289		
	5%, 95%	0.011, 0.500			0.028, 0.195		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 9 of 264)

Biomarker: NNAL (pg/mL)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	121.7, 84.9	6.5, 6.2		166.0, 120.8	6.3, 6.2	
	SD, SE	83.64, 19.71	2.61, 0.48		116.66, 20.62	0.93, 0.16	
	MEDIAN	127.5	6.0		150.8	6.0	
	MIN, MAX	6.0, 333.0	6.0, 20.3		6.0, 484.5	6.0, 9.6	
	5%, 95%	6.0, 333.0	6.0, 6.0		11.4, 463.9	6.0, 9.6	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	122.7, 89.1	8.7, 7.1		183.8, 149.5	6.1, 6.1	
	SD, SE	81.19, 19.69	9.14, 1.67		118.10, 21.93	0.76, 0.13	
	MEDIAN	134.6	6.0		160.8	6.0	
	MIN, MAX	6.0, 290.8	6.0, 42.4		28.2, 485.1	6.0, 10.5	
	5%, 95%	6.0, 290.8	6.0, 40.7		45.6, 411.9	6.0, 6.0	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	122.7, 92.8	7.6, 6.9		171.2, 135.6	6.2, 6.2	
	SD, SE	68.42, 16.13	4.69, 0.86		112.66, 19.92	0.59, 0.10	
	MEDIAN	135.9	6.0		152.1	6.0	
	MIN, MAX	6.0, 233.8	6.0, 24.2		17.1, 474.5	6.0, 8.3	
	5%, 95%	6.0, 233.8	6.0, 23.4		28.5, 444.8	6.0, 7.8	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 10 of 264)

Biomarker: NNAL (pmol/L)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	581.6, 405.8	31.0, 29.9		793.5, 577.7	30.0, 29.8	
	SD, SE	399.78, 94.23	12.47, 2.28		557.62, 98.57	4.45, 0.75	
	MEDIAN	609.5	28.7		720.6	28.7	
	MIN, MAX	28.7, 1591.7	28.7, 97.0		28.7, 2315.9	28.7, 45.9	
	5%, 95%	28.7, 1591.7	28.7, 28.7		54.5, 2217.4	28.7, 45.9	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	586.3, 426.0	41.7, 33.8		878.5, 714.7	29.3, 29.2	
	SD, SE	388.07, 94.12	43.66, 7.97		564.50, 104.82	3.63, 0.61	
	MEDIAN	643.4	28.7		768.6	28.7	
	MIN, MAX	28.7, 1390.0	28.7, 202.7		134.8, 2318.8	28.7, 50.2	
	5%, 95%	28.7, 1390.0	28.7, 194.5		218.0, 1968.9	28.7, 28.7	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	586.6, 443.3	36.4, 33.0		818.0, 648.1	29.7, 29.6	
	SD, SE	327.02, 77.08	22.37, 4.08		538.54, 95.20	2.81, 0.47	
	MEDIAN	649.5	28.7		726.7	28.7	
	MIN, MAX	28.7, 1117.6	28.7, 115.7		81.8, 2268.1	28.7, 39.5	
	5%, 95%	28.7, 1117.6	28.7, 111.6		136.3, 2126.2	28.7, 37.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 11 of 264)

Biomarker: NNAL ((pg/mL)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	9.1, 6.7			12.1, 9.2		
	SD, SE	7.55, 1.78			9.92, 1.75		
	MEDIAN	7.2			8.5		
	MIN, MAX	1.4, 27.8			1.9, 47.0		
	5%, 95%	1.4, 27.8			2.9, 34.8		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	12.1, 8.4			13.4, 10.8		
	SD, SE	13.33, 3.23			9.40, 1.75		
	MEDIAN	8.9			11.4		
	MIN, MAX	2.0, 58.2			3.8, 38.5		
	5%, 95%	2.0, 58.2			4.3, 31.2		
	# of BLQ/ALQ Values	1/0			0/0		
Overall [*]	N	18		NA	32		NA
	MEAN, GEO MEAN	10.4, 7.9			13.2, 10.5		
	SD, SE	9.27, 2.18			9.97, 1.76		
	MEDIAN	8.2			10.0		
	MIN, MAX	2.0, 42.4			3.7, 47.0		
	5%, 95%	2.0, 42.4			4.1, 36.7		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 12 of 264)

Biomarker: NNAL ((pmol/L)/cigarette per day)		Analytical Lab: Madison				
Timepoint	Statistic	Male		P-value*	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	18		NA	32	NA
	MEAN, GEO MEAN	43.3, 32.0			57.7, 43.8	
	SD, SE	36.05, 8.50			47.46, 8.39	
	MEDIAN	34.4			40.6	
	MIN, MAX	6.5, 132.6			9.0, 224.7	
	5%, 95%	6.5, 132.6			13.6, 166.3	
Week 3	# of BLQ/ALQ Values	1/0			1/0	
	N	17		NA	29	NA
	MEAN, GEO MEAN	57.7, 40.1			64.1, 51.7	
	SD, SE	63.66, 15.44			44.91, 8.34	
	MEDIAN	42.5			54.4	
	MIN, MAX	9.6, 278.0			18.2, 183.9	
Overall*	5%, 95%	9.6, 278.0			20.6, 148.9	
	# of BLQ/ALQ Values	1/0			0/0	
	N	18		NA	32	NA
	MEAN, GEO MEAN	49.7, 37.5			62.8, 50.1	
	SD, SE	44.25, 10.43			47.64, 8.42	
	MEDIAN	39.1			47.4	
	MIN, MAX	9.6, 202.5			17.7, 224.7	
	5%, 95%	9.6, 202.5			19.4, 175.1	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 13 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/24hr)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	803982.853, 509039.708	17773.167, 11018.595		890920.641, 630563.563	11732.457, 10761.183	
	SD, SE	609148.1353, 147740.1237	32167.6563, 5872.9837		623305.8737, 110185.9525	4713.9363, 796.8007	
	MEDIAN	529126.000	8940.000		801427.000	11100.000	
	MIN, MAX	8460.000, 2084332.500	3180.000, 181986.000		34650.000, 2307613.000	3420.000, 20100.000	
	5%, 95%	8460.000, 2084332.500	3900.000, 41624.000		37125.000, 2245880.000	4800.000, 19500.000	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	780888.882, 484578.381	13735.533, 11563.274		992757.038, 730891.571	14912.257, 12932.435	
	SD, SE	625370.0458, 151674.5149	10652.3865, 1944.8508		753692.7111, 139957.2229	10344.7620, 1748.5839	
	MEDIAN	540730.000	10740.000		928092.000	12180.000	
	MIN, MAX	6288.000, 2075948.000	4500.000, 61490.000		56730.000, 4046406.000	5940.000, 53066.000	
	5%, 95%	6288.000, 2075948.000	4500.000, 28208.000		97520.000, 1962480.000	6408.000, 50799.000	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	803959.736, 518625.587	15754.350, 11765.827		914025.181, 677520.375	13322.357, 12146.527	
	SD, SE	602618.8956, 142038.6358	17937.3794, 3274.9024		592842.6716, 104800.7683	6356.8366, 1074.5015	
	MEDIAN	619903.500	9780.000		855139.500	11790.000	
	MIN, MAX	7374.000, 2080140.250	3840.000, 97218.000		46927.500, 2468208.000	6400.000, 33874.500	
	5%, 95%	7374.000, 2080140.250	4590.000, 51557.000		66085.000, 2135046.500	6450.000, 30583.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 14 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/24hr) Analytical Lab: Madison

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3843.038, 2433.210	84.956, 52.669		4258.601, 3014.094	56.081, 51.439	
	SD, SE	2911.7280, 706.1978	153.7614, 28.0729		2979.4020, 526.6888	22.5326, 3.8087	
	MEDIAN	2529.222	42.733		3830.821	53.058	
	MIN, MAX	40.439, 9963.109	15.200, 869.893		165.627, 11030.390	16.348, 96.078	
	5%, 95%	40.439, 9963.109	18.642, 198.963		177.458, 10735.306	22.944, 93.210	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	3732.649, 2316.286	65.656, 55.272		4745.379, 3493.662	71.281, 61.817	
	SD, SE	2989.2688, 725.0042	50.9184, 9.2964		3602.6512, 668.9955	49.4479, 8.3582	
	MEDIAN	2584.689	51.337		4436.280	58.220	
	MIN, MAX	30.057, 9923.031	21.510, 293.922		271.169, 19341.821	28.393, 253.655	
	5%, 95%	30.057, 9923.031	21.510, 134.834		466.146, 9380.654	30.630, 242.819	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3842.928, 2479.032	75.306, 56.241		4369.041, 3238.548	63.681, 58.061	
	SD, SE	2880.5182, 678.9446	85.7407, 15.6540		2833.7879, 500.9477	30.3856, 5.1361	
	MEDIAN	2963.139	46.749		4087.567	56.357	
	MIN, MAX	35.248, 9943.070	18.355, 464.702		224.314, 11798.035	30.592, 161.920	
	5%, 95%	35.248, 9943.070	21.940, 246.443		315.887, 10205.522	30.831, 146.187	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 15 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/24hr)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	54121.155, 38734.348			57697.510, 47747.375		
	SD, SE	42632.2867, 10339.8483			37505.6610, 6630.1268		
	MEDIAN	35036.000			50712.529		
	MIN, MAX	2820.000, 171072.000			8662.500, 176718.500		
	5%, 95%	2820.000, 171072.000			15822.400, 153840.867		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	60028.332, 45578.426			64148.130, 52875.770		
	SD, SE	36477.1862, 8847.0172			43424.9009, 8063.8017		
	MEDIAN	57631.857			49703.125		
	MIN, MAX	2096.000, 138353.600			14182.500, 192686.000		
	5%, 95%	2096.000, 138353.600			18154.500, 172716.667		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	57103.365, 44343.694			61047.286, 52314.024		
	SD, SE	35431.8491, 8351.3669			33743.8833, 5965.1322		
	MEDIAN	52277.687			51637.690		
	MIN, MAX	2458.000, 154712.800			16372.500, 142336.434		
	5%, 95%	2458.000, 154712.800			16521.250, 132624.738		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439183

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 16 of 264)

Biomarker: NNAL plus NNAL-gluc ((pmol/24hr)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	258.699, 185.151			275.794, 228.233		
	SD, SE	203.7822, 49.4245			179.2769, 31.6920		
	MEDIAN	167.472			242.406		
	MIN, MAX	13.480, 817.724			41.407, 844.714		
	5%, 95%	13.480, 817.724			75.631, 735.359		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	286.935, 217.865			306.628, 252.746		
	SD, SE	174.3609, 42.2887			207.5710, 38.5450		
	MEDIAN	275.480			237.581		
	MIN, MAX	10.019, 661.330			67.792, 921.039		
	5%, 95%	10.019, 661.330			86.779, 825.586		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	272.954, 211.964			291.806, 250.061		
	SD, SE	169.3642, 39.9195			161.2956, 28.5133		
	MEDIAN	249.888			246.829		
	MIN, MAX	11.750, 739.527			78.261, 680.368		
	5%, 95%	11.750, 739.527			78.972, 633.946		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 17 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mg Creatinine)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	632.351, 388.963	11.176, 6.201		794.208, 549.931	10.028, 9.133	
	SD, SE	604.3903, 146.5862	23.9321, 4.3694		576.5665, 101.9235	4.0580, 0.6859	
	MEDIAN	339.746	5.013		629.249	9.509	
	MIN, MAX	7.958, 2575.145	1.932, 134.956		18.519, 2476.718	2.285, 18.634	
	5%, 95%	7.958, 2575.145	2.103, 25.707		30.892, 2010.238	3.883, 17.699	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	533.334, 349.698	7.775, 6.330		832.490, 623.362	13.535, 11.212	
	SD, SE	387.2534, 93.9228	6.1746, 1.1273		567.0182, 105.2926	10.2695, 1.7350	
	MEDIAN	381.623	6.049		634.698	10.657	
	MIN, MAX	5.525, 1261.017	2.158, 34.375		56.481, 2275.640	3.259, 53.767	
	5%, 95%	5.525, 1261.017	2.413, 15.074		65.031, 2024.775	3.795, 41.549	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	581.550, 377.045	9.476, 6.637		808.453, 587.104	11.781, 10.488	
	SD, SE	470.7092, 110.9472	12.6956, 2.3179		554.2552, 97.9794	6.1400, 1.0378	
	MEDIAN	389.237	5.327		654.457	10.520	
	MIN, MAX	6.742, 1877.496	2.131, 70.371		41.775, 2250.747	3.634, 30.459	
	5%, 95%	6.742, 1877.496	2.364, 30.041		43.687, 2007.510	4.739, 27.562	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 18 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/mg Creatinine)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3.023, 1.859	0.033, 0.030		3.796, 2.629	0.048, 0.044	
	SD, SE	2.8890, 0.7007	0.1144, 0.0209		2.7560, 0.4872	0.0194, 0.0033	
	MEDIAN	1.624	0.024		3.008	0.045	
	MIN, MAX	0.038, 12.309	0.009, 0.645		0.089, 11.839	0.011, 0.089	
	5%, 95%	0.038, 12.309	0.010, 0.123		0.148, 9.609	0.019, 0.085	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2.549, 1.670	0.037, 0.030		3.979, 2.980	0.065, 0.054	
	SD, SE	1.8512, 0.4490	0.0295, 0.0054		2.7104, 0.5033	0.0491, 0.0083	
	MEDIAN	1.824	0.029		3.034	0.051	
	MIN, MAX	0.026, 6.028	0.010, 0.164		0.270, 10.878	0.016, 0.257	
	5%, 95%	0.026, 6.028	0.012, 0.072		0.311, 9.678	0.018, 0.199	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2.780, 1.802	0.046, 0.032		3.865, 2.807	0.057, 0.050	
	SD, SE	2.2501, 0.5304	0.0608, 0.0111		2.6493, 0.4683	0.0293, 0.0049	
	MEDIAN	1.861	0.026		3.129	0.051	
	MIN, MAX	0.032, 8.975	0.010, 0.337		0.200, 10.759	0.018, 0.146	
	5%, 95%	0.032, 8.975	0.011, 0.144		0.209, 9.596	0.023, 0.132	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 19 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mg Creatinine)/cigarette per day Analytical Lab: Madison

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	60.839, 29.598			50.350, 41.642		
	SD, SE	118.7808, 28.8086			31.1852, 5.5128		
	MEDIAN	29.102			41.206		
	MIN, MAX	2.653, 515.029			4.630, 134.016		
	5%, 95%	2.653, 515.029			15.446, 116.939		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	48.034, 32.892			55.315, 45.097		
	SD, SE	51.9735, 12.6054			39.5695, 7.3479		
	MEDIAN	34.062			45.436		
	MIN, MAX	1.842, 235.969			14.120, 164.956		
	5%, 95%	1.842, 235.969			16.258, 155.193		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	53.182, 32.225			53.855, 45.461		
	SD, SE	82.3686, 19.4145			32.3057, 5.7109		
	MEDIAN	29.297			43.072		
	MIN, MAX	2.248, 375.499			10.444, 133.834		
	5%, 95%	2.248, 375.499			14.783, 131.185		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	0.291, 0.142			0.241, 0.199		
	SD, SE	0.5678, 0.1377			0.1490, 0.0263		
	MEDIAN	0.139			0.198		
	MIN, MAX	0.013, 2.462			0.022, 0.641		
	5%, 95%	0.013, 2.462			0.074, 0.559		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.230, 0.157			0.265, 0.216		
	SD, SE	0.2484, 0.0603			0.1891, 0.0351		
	MEDIAN	0.163			0.217		
	MIN, MAX	0.009, 1.128			0.068, 0.789		
	5%, 95%	0.009, 1.128			0.078, 0.742		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.255, 0.155			0.258, 0.218		
	SD, SE	0.3937, 0.0928			0.1543, 0.0273		
	MEDIAN	0.140			0.206		
	MIN, MAX	0.011, 1.795			0.050, 0.640		
	5%, 95%	0.011, 1.795			0.071, 0.627		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pg/mL)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	532.4, 308.3	13.7, 7.5		554.4, 360.2	6.0, 6.0	
	SD, SE	500.33, 121.35	33.35, 6.09		459.48, 81.23	0.17, 0.03	
	MEDIAN	445.5	6.0		484.0	6.0	
	MIN, MAX	6.0, 1773.9	6.0, 185.7		13.5, 2045.7	6.0, 7.0	
	5%, 95%	6.0, 1773.9	6.0, 47.3		16.5, 1604.2	6.0, 6.0	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	427.5, 286.6	7.5, 6.6		626.3, 425.9	7.2, 6.6	
	SD, SE	313.45, 76.02	7.53, 1.38		557.17, 103.46	4.74, 0.80	
	MEDIAN	415.9	6.0		482.0	6.0	
	MIN, MAX	6.0, 1235.3	6.0, 47.3		30.5, 2223.3	6.0, 31.4	
	5%, 95%	6.0, 1235.3	6.0, 8.6		53.0, 1842.9	6.0, 17.7	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	486.9, 321.5	10.6, 7.3		573.7, 393.7	6.6, 6.4	
	SD, SE	362.20, 85.37	17.77, 3.24		462.07, 81.68	2.37, 0.40	
	MEDIAN	385.6	6.0		453.3	6.0	
	MIN, MAX	6.0, 1230.7	6.0, 95.9		22.0, 1663.1	6.0, 18.7	
	5%, 95%	6.0, 1230.7	6.0, 47.3		34.8, 1653.7	6.0, 11.9	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (pmol/L)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2544.7, 1473.7	65.3, 35.9		2650.1, 1721.5	28.8, 28.8	
	SD, SE	2391.57, 580.04	159.42, 29.11		2196.31, 388.26	0.81, 0.14	
	MEDIAN	2129.5	28.7		2313.3	28.7	
	MIN, MAX	28.7, 8479.2	28.7, 887.6		64.5, 9778.4	28.7, 33.5	
	5%, 95%	28.7, 8479.2	28.7, 226.1		78.9, 7668.1	28.7, 28.7	
	# of BLQ/ALQ Values	1/0	24/0		0/0	34/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2043.4, 1370.0	36.1, 31.5		2993.7, 2035.8	34.6, 31.6	
	SD, SE	1498.29, 363.39	36.01, 6.57		2663.28, 494.56	22.66, 3.83	
	MEDIAN	1988.0	28.7		2304.0	28.7	
	MIN, MAX	28.7, 5904.7	28.7, 226.1		145.8, 10627.4	28.7, 150.1	
	5%, 95%	28.7, 5904.7	28.7, 41.1		253.3, 8809.1	28.7, 84.6	
	# of BLQ/ALQ Values	1/0	26/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2327.4, 1536.6	50.7, 34.9		2742.2, 1881.7	31.7, 30.6	
	SD, SE	1731.30, 408.07	84.92, 15.50		2208.67, 390.44	11.32, 1.91	
	MEDIAN	1843.1	28.7		2166.6	28.7	
	MIN, MAX	28.7, 5882.5	28.7, 458.2		105.2, 7949.4	28.7, 89.4	
	5%, 95%	28.7, 5882.5	28.7, 226.1		166.1, 7904.4	28.7, 56.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pg/mL)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	35.9, 23.5			36.1, 27.3		
	SD, SE	33.16, 8.04			27.44, 4.85		
	MEDIAN	27.3			26.7		
	MIN, MAX	2.0, 128.6			4.1, 109.3		
	5%, 95%	2.0, 128.6			6.8, 95.6		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	43.2, 27.0			41.2, 30.8		
	SD, SE	56.18, 13.62			31.58, 5.86		
	MEDIAN	25.2			23.7		
	MIN, MAX	2.0, 247.1			7.6, 105.9		
	5%, 95%	2.0, 247.1			10.0, 100.6		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	39.2, 27.3			39.2, 30.4		
	SD, SE	37.94, 8.94			28.33, 5.01		
	MEDIAN	31.4			26.1		
	MIN, MAX	2.0, 168.1			7.2, 109.3		
	5%, 95%	2.0, 168.1			8.7, 98.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc (tpmol/L/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	171.7, 112.2			172.4, 130.4		
	SD, SE	158.49, 38.44			131.15, 23.18		
	MEDIAN	130.7			127.8		
	MIN, MAX	9.6, 614.6			19.7, 522.5		
	5%, 95%	9.6, 614.6			32.3, 456.7		
	# of BLQ/ALQ Values	1/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	206.4, 128.9			196.8, 147.3		
	SD, SE	268.48, 65.12			151.02, 28.04		
	MEDIAN	120.5			113.4		
	MIN, MAX	9.6, 1180.9			36.5, 506.1		
	5%, 95%	9.6, 1180.9			47.7, 481.1		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	187.5, 130.6			187.3, 145.1		
	SD, SE	181.30, 42.73			135.44, 23.94		
	MEDIAN	149.8			124.8		
	MIN, MAX	9.6, 803.4			34.4, 522.5		
	5%, 95%	9.6, 803.4			41.5, 468.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide (pmol/L)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	29	<.0001	32	32	<.0001
	MEAN, GEO MEAN	1950.1, NA	37.9, NA		1856.6, 1069.4	0.2, NA	
	SD, SE	2050.37, 497.29	162.11, 30.10		1691.41, 299.00	0.85, 0.15	
	MEDIAN	1543.0	0.0		1631.9	0.0	
	MIN, MAX	0.0, 7358.3	0.0, 859.0		24.4, 7462.5	0.0, 4.8	
	5%, 95%	0.0, 7358.3	0.0, 197.4		35.9, 5458.8	0.0, 0.0	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	28	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1457.1, NA	2.0, NA		2115.3, 1152.9	5.3, NA	
	SD, SE	1136.78, 275.71	6.52, 1.23		2223.97, 412.98	19.50, 3.30	
	MEDIAN	1234.2	0.0		1443.6	0.0	
	MIN, MAX	0.0, 4514.7	0.0, 31.5		11.0, 9536.6	0.0, 99.9	
	5%, 95%	0.0, 4514.7	0.0, 12.4		35.4, 7004.1	0.0, 55.9	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1744.6, NA	19.2, NA		1924.2, 1135.3	2.7, NA	
	SD, SE	1455.58, 343.08	80.23, 14.65		1730.55, 305.92	9.75, 1.65	
	MEDIAN	1277.7	0.0		1626.1	0.0	
	MIN, MAX	0.0, 4879.9	0.0, 429.5		23.5, 5778.3	0.0, 50.0	
	5%, 95%	0.0, 4879.9	0.0, 114.5		29.9, 5681.3	0.0, 28.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL-O-glucuronide ((pmol/L)/cigarette per day) Analytical Lab: Madison

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	128.9, NA			114.7, 81.0		
	SD, SE	125.32, 30.39			92.49, 16.35		
	MEDIAN	85.7			86.2		
	MIN, MAX	0.0, 481.9			6.1, 363.9		
	5%, 95%	0.0, 481.9			16.9, 339.2		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	148.7, NA			132.7, 83.5		
	SD, SE	206.23, 50.02			117.49, 21.82		
	MEDIAN	80.1			77.7		
	MIN, MAX	0.0, 902.9			2.8, 454.1		
	5%, 95%	0.0, 902.9			8.9, 350.2		
	# of BLQ/ALQ Values	1/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	138.3, NA			124.6, 88.0		
	SD, SE	139.15, 32.80			96.22, 17.01		
	MEDIAN	107.8			86.6		
	MIN, MAX	0.0, 601.0			7.5, 356.9		
	5%, 95%	0.0, 601.0			10.4, 306.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 27 of 264)

Biomarker: NNAL-O-glucuronide (pmol/24hr)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	29	<.0001	32	32	<.0001
	MEAN, GEO MEAN	2904.964, NA	38.243, NA		2911.039, 1872.337	0.147, NA	
	SD, SE	2489.6679, 603.8332	158.0832, 29.3553		2191.8620, 387.4701	0.8316, 0.1470	
	MEDIAN	1833.188	0.000		2516.876	0.000	
	MIN, MAX	0.000, 8646.003	0.000, 841.820		51.240, 8788.668	0.000, 4.704	
	5%, 95%	0.000, 8646.003	0.000, 173.712		98.725, 7630.840	0.000, 0.000	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	28	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2636.817, NA	3.352, NA		3277.052, 1978.544	10.165, NA	
	SD, SE	2140.5686, 519.1641	10.3068, 1.9478		3205.0765, 595.1678	38.8545, 6.5676	
	MEDIAN	1703.196	0.000		2646.905	0.000	
	MIN, MAX	0.000, 7252.530	0.000, 40.950		20.460, 17356.612	0.000, 168.831	
	5%, 95%	0.000, 7252.530	0.000, 36.120		65.136, 6821.100	0.000, 160.433	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2839.652, NA	20.049, NA		2996.589, 1953.512	5.150, NA	
	SD, SE	2316.2775, 545.9518	78.3074, 14.2969		2267.1090, 400.7720	19.4133, 3.2815	
	MEDIAN	2120.435	0.000		2644.194	0.000	
	MIN, MAX	0.000, 7949.267	0.000, 420.910		58.188, 10073.384	0.000, 84.416	
	5%, 95%	0.000, 7949.267	0.000, 107.331		59.593, 7804.884	0.000, 80.217	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 28 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/24hr)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	191.695, NA			178.194, 141.777		
	SD, SE	154.3645, 37.4389			119.7548, 21.1699		
	MEDIAN	120.232			165.201		
	MIN, MAX	0.000, 574.157			12.810, 585.911		
	5%, 95%	0.000, 574.157			47.073, 437.301		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	203.742, NA			201.878, 143.136		
	SD, SE	132.0991, 32.0387			168.0591, 31.2078		
	MEDIAN	168.115			147.793		
	MIN, MAX	0.000, 505.646			5.115, 826.505		
	5%, 95%	0.000, 505.646			16.284, 517.290		
	# of BLQ/ALQ Values	1/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	198.934, NA			189.637, 151.404		
	SD, SE	129.3352, 30.4846			118.5019, 20.9484		
	MEDIAN	165.534			166.137		
	MIN, MAX	0.000, 539.902			14.547, 520.326		
	5%, 95%	0.000, 539.902			27.239, 476.665		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 29 of 264)

Biomarker: NNAL-O-glucuronide (pmol/mg Creatinine)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17	29	<.0001	32	32	<.0001
	MEAN, GEO MEAN	2.232, NA	0.027, NA		2.590, 1.632	0.000, NA	
	SD, SE	2.1168, 0.5134	0.1166, 0.0217		2.0000, 0.3535	0.0005, 0.0001	
	MEDIAN	1.190	0.000		2.237	0.000	
	MIN, MAX	0.000, 8.643	0.000, 0.624		0.027, 7.951	0.000, 0.003	
	5%, 95%	0.000, 8.643	0.000, 0.107		0.082, 7.656	0.000, 0.000	
	# of BLQ/ALQ Values	1/0	29/0		1/0	32/0	
Week 3	N	17	28	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1.818, NA	0.002, NA		2.688, 1.686	0.009, NA	
	SD, SE	1.3733, 0.3331	0.0056, 0.0011		2.1935, 0.4073	0.0359, 0.0061	
	MEDIAN	1.355	0.000		1.939	0.000	
	MIN, MAX	0.000, 4.312	0.000, 0.023		0.020, 9.761	0.000, 0.171	
	5%, 95%	0.000, 4.312	0.000, 0.019		0.043, 6.968	0.000, 0.131	
	# of BLQ/ALQ Values	1/0	27/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2.037, NA	0.014, NA		2.618, 1.692	0.005, NA	
	SD, SE	1.6980, 0.4002	0.0576, 0.0105		1.9471, 0.3442	0.0181, 0.0031	
	MEDIAN	1.169	0.000		2.014	0.000	
	MIN, MAX	0.000, 6.478	0.000, 0.312		0.035, 7.312	0.000, 0.086	
	5%, 95%	0.000, 6.478	0.000, 0.065		0.051, 7.084	0.000, 0.066	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 30 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/mg Creatinine)/cigarette per day) Analytical Lab: Madison

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	17		NA	32		NA
	MEAN, GEO MEAN	0.211, NA			0.156, 0.124		
	SD, SE	0.3990, 0.0968			0.1057, 0.0187		
	MEDIAN	0.119			0.125		
	MIN, MAX	0.000, 1.729			0.007, 0.510		
	5%, 95%	0.000, 1.729			0.041, 0.364		
	# of BLQ/ALQ Values	1/0			1/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.165, NA			0.170, 0.122		
	SD, SE	0.1919, 0.0466			0.1322, 0.0245		
	MEDIAN	0.108			0.122		
	MIN, MAX	0.000, 0.862			0.005, 0.494		
	5%, 95%	0.000, 0.862			0.011, 0.465		
	# of BLQ/ALQ Values	1/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	0.184, NA			0.166, 0.132		
	SD, SE	0.2853, 0.0672			0.1068, 0.0189		
	MEDIAN	0.103			0.140		
	MIN, MAX	0.000, 1.296			0.009, 0.488		
	5%, 95%	0.000, 1.296			0.023, 0.364		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 31 of 264)

Biomarker: Cotinine (ug/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1683.977, 1226.756	4.187, 2.268		1833.759, 1377.866	2.289, 1.974	
	SD, SE	920.8075, 217.0364	6.2628, 1.1434		1274.5169, 225.3049	1.3989, 0.2365	
	MEDIAN	1908.816	1.830		1583.006	1.950	
	MIN, MAX	26.790, 3201.831	0.530, 27.900		50.050, 6435.660	0.570, 6.912	
	5%, 95%	26.790, 3201.831	0.715, 20.140		308.979, 3606.938	0.800, 6.825	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1784.287, 1256.439	5.196, 2.549		1837.173, 1433.924	2.387, 2.083	
	SD, SE	902.3151, 212.6777	10.7544, 1.9635		1174.1091, 210.8762	1.3526, 0.2286	
	MEDIAN	1769.274	1.917		1686.630	2.200	
	MIN, MAX	13.950, 3133.273	0.625, 59.280		148.738, 4366.890	0.660, 7.795	
	5%, 95%	13.950, 3133.273	0.815, 13.221		350.900, 4252.954	0.750, 4.875	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2040.610, 1231.977	3.809, 2.464		1902.946, 1558.715	2.248, 2.050	
	SD, SE	1576.7984, 382.4298	5.2300, 0.9549		1132.3107, 210.2648	1.0814, 0.1828	
	MEDIAN	1600.536	2.032		1655.220	2.050	
	MIN, MAX	6.393, 5162.740	0.750, 25.870		225.246, 4886.167	0.940, 6.420	
	5%, 95%	6.393, 5162.740	1.072, 15.370		391.688, 3866.576	0.990, 4.740	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^a	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1830.019, 1303.963	4.397, 2.599		1818.890, 1460.495	2.308, 2.091	
	SD, SE	1019.6382, 240.3310	6.2744, 1.1455		1095.3362, 193.6299	1.0681, 0.1805	
	MEDIAN	1786.237	1.991		1681.960	2.150	
	MIN, MAX	15.711, 3774.690	0.787, 30.043		141.345, 4483.278	0.967, 5.145	
	5%, 95%	15.711, 3774.690	1.092, 16.027		374.266, 3982.288	0.980, 4.770	

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 32 of 264)

Biomarker: Cotinine (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9556.568, 6961.841	23.762, 12.871		10406.583, 7819.392	12.989, 11.201	
	SD, SE	5225.5828, 1231.6817	35.5415, 6.4890		7232.8836, 1278.6053	7.9390, 1.3419	
	MEDIAN	10832.531	10.383		8983.556	11.066	
	MIN, MAX	152.033, 18170.391	3.008, 158.333		284.034, 36522.371	3.235, 39.226	
	5%, 95%	152.033, 18170.391	4.058, 114.295		1753.456, 20469.373	4.540, 38.732	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	10125.830, 7130.292	29.490, 14.465		10425.957, 8137.517	13.549, 11.824	
	SD, SE	5120.6381, 1206.9460	61.0312, 11.1427		6663.0694, 1196.7226	7.6759, 1.2975	
	MEDIAN	10040.630	10.879		9571.625	12.485	
	MIN, MAX	79.166, 17781.324	3.547, 336.414		844.088, 24782.101	3.746, 44.237	
	5%, 95%	79.166, 17781.324	4.625, 75.029		1991.358, 24135.514	4.256, 27.666	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	11580.459, 6991.468	21.615, 13.985		10799.218, 8845.710	12.756, 11.636	
	SD, SE	8948.3309, 2170.2890	29.6804, 5.4189		6425.8632, 1193.2528	6.1368, 1.0373	
	MEDIAN	9083.042	11.532		9393.374	11.634	
	MIN, MAX	36.280, 29298.550	4.256, 146.812		1278.271, 27728.998	5.335, 36.434	
	5%, 95%	36.280, 29298.550	6.084, 87.225		2222.829, 21942.819	5.618, 26.900	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	10385.356, 7399.989	24.956, 14.747		10322.202, 8288.311	13.098, 11.867	
	SD, SE	5786.4474, 1363.8787	35.6075, 6.5010		6216.0336, 1098.8499	6.0612, 1.0245	
	MEDIAN	10136.892	11.298		9545.122	12.201	
	MIN, MAX	89.160, 21421.368	4.464, 170.496		802.131, 25442.605	5.486, 29.198	
	5%, 95%	89.160, 21421.368	6.195, 90.955		2123.957, 22599.486	5.562, 27.068	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 33 of 264)

Biomarker: Cotinine ((µg/24hr/cigarette per day) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	125.049, 96.672			134.139, 104.334		
	SD, SE	89.1273, 21.0075			118.9202, 21.0223		
	MEDIAN	101.557			98.981		
	MIN, MAX	8.930, 385.805			25.025, 643.566		
	5%, 95%	8.930, 385.805			29.911, 304.113		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	173.708, 99.521			145.277, 116.936		
	SD, SE	287.4993, 67.7642			105.1783, 18.8906		
	MEDIAN	117.995			107.678		
	MIN, MAX	4.650, 1308.045			32.188, 485.210		
	5%, 95%	4.650, 1308.045			41.747, 342.365		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	155.573, 115.877			135.216, 112.764		
	SD, SE	81.4576, 19.7564			89.9849, 16.7098		
	MEDIAN	160.120			111.844		
	MIN, MAX	2.131, 320.107			45.833, 335.938		
	5%, 95%	2.131, 320.107			46.306, 330.911		
	# of BLQ/ALQ Values	0/0			0/0		
Overall [*]	N	18		NA	32		NA
	MEAN, GEO MEAN	150.028, 108.591			137.396, 115.621		
	SD, SE	140.5316, 33.1236			94.0927, 16.6334		
	MEDIAN	118.237			102.109		
	MIN, MAX	5.237, 671.319			47.120, 486.562		
	5%, 95%	5.237, 671.319			48.557, 299.233		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 34 of 264)

Biomarker: Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	709.652, 548.614			761.351, 592.098		
	SD, SE	505.7971, 119.2175			674.8723, 119.3017		
	MEDIAN	576.335			561.716		
	MIN, MAX	50.678, 2189.442			142.017, 3652.237		
	5%, 95%	50.678, 2189.442			169.746, 1725.843		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	985.790, 564.781			824.446, 663.612		
	SD, SE	1631.5586, 384.5620			596.8868, 107.2040		
	MEDIAN	669.619			611.073		
	MIN, MAX	26.389, 7423.156			182.668, 2753.567		
	5%, 95%	26.389, 7423.156			236.913, 1942.924		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	882.879, 657.602			767.351, 639.936		
	SD, SE	462.2721, 112.1175			510.6639, 94.8279		
	MEDIAN	908.683			634.712		
	MIN, MAX	12.093, 1816.608			260.099, 1906.445		
	5%, 95%	12.093, 1816.608			262.788, 1877.918		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	851.411, 616.255			779.721, 656.148		
	SD, SE	797.5169, 187.9765			533.9762, 94.3945		
	MEDIAN	670.996			579.469		
	MIN, MAX	29.720, 3809.735			267.406, 2761.241		
	5%, 95%	29.720, 3809.735			275.561, 1698.146		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine (µg/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.448, 0.928	0.003, NA		1.697, 1.202	0.002, NA	
	SD, SE	1.3218, 0.3115	0.0041, 0.0008		1.1734, 0.2074	0.0017, 0.0003	
	MEDIAN	1.260	0.001		1.628	0.002	
	MIN, MAX	0.025, 5.808	0.000, 0.020		0.042, 4.207	0.000, 0.010	
	5%, 95%	0.025, 5.808	0.000, 0.010		0.203, 3.903	0.001, 0.005	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1.431, 0.925	0.004, NA		1.499, 1.139	0.002, NA	
	SD, SE	1.1733, 0.2765	0.0102, 0.0019		1.0524, 0.1890	0.0014, 0.0002	
	MEDIAN	1.264	0.001		1.250	0.002	
	MIN, MAX	0.016, 5.177	0.000, 0.057		0.148, 4.123	0.000, 0.007	
	5%, 95%	0.016, 5.177	0.000, 0.007		0.275, 3.337	0.001, 0.005	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1.378, 0.893	0.002, NA		1.745, 1.329	0.002, 0.002	
	SD, SE	0.9164, 0.2223	0.0028, 0.0005		1.3149, 0.2442	0.0015, 0.0003	
	MEDIAN	1.292	0.001		1.410	0.002	
	MIN, MAX	0.006, 3.315	0.000, 0.014		0.224, 5.186	0.001, 0.009	
	5%, 95%	0.006, 3.315	0.000, 0.009		0.383, 4.641	0.001, 0.005	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.412, 0.957	0.003, NA		1.666, 1.253	0.002, NA	
	SD, SE	1.0606, 0.2500	0.0049, 0.0009		1.1632, 0.2056	0.0013, 0.0002	
	MEDIAN	1.295	0.001		1.349	0.002	
	MIN, MAX	0.016, 4.572	0.000, 0.026		0.138, 4.505	0.000, 0.006	
	5%, 95%	0.016, 4.572	0.001, 0.009		0.266, 3.886	0.001, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 36 of 264)

Biomarker: Cotinine (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	8.216, 5.264	0.015, NA		9.630, 6.822	0.012, NA	
	SD, SE	7.5011, 1.7680	0.0234, 0.0043		6.6590, 1.1772	0.0094, 0.0016	
	MEDIAN	7.151	0.006		9.239	0.011	
	MIN, MAX	0.142, 32.960	0.000, 0.114		0.238, 23.875	0.000, 0.057	
	5%, 95%	0.142, 32.960	0.000, 0.057		1.152, 22.150	0.006, 0.028	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	8.122, 5.249	0.022, NA		8.506, 6.461	0.012, NA	
	SD, SE	6.6582, 1.5693	0.0577, 0.0105		5.9724, 1.0727	0.0080, 0.0013	
	MEDIAN	7.174	0.006		7.094	0.011	
	MIN, MAX	0.091, 29.379	0.000, 0.323		0.840, 23.398	0.000, 0.040	
	5%, 95%	0.091, 29.379	0.000, 0.040		1.561, 18.937	0.006, 0.028	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	7.819, 5.065	0.012, NA		9.903, 7.544	0.012, 0.010	
	SD, SE	5.2007, 1.2614	0.0158, 0.0029		7.4619, 1.3856	0.0087, 0.0015	
	MEDIAN	7.332	0.006		8.002	0.011	
	MIN, MAX	0.034, 18.813	0.000, 0.079		1.271, 29.431	0.006, 0.051	
	5%, 95%	0.034, 18.813	0.000, 0.051		2.174, 26.338	0.006, 0.028	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	8.016, 5.428	0.017, NA		9.455, 7.113	0.012, 0.010	
	SD, SE	6.0188, 1.4186	0.0278, 0.0051		6.6015, 1.1670	0.0073, 0.0012	
	MEDIAN	7.346	0.008		7.653	0.009	
	MIN, MAX	0.089, 25.944	0.000, 0.149		0.783, 25.568	0.002, 0.036	
	5%, 95%	0.089, 25.944	0.004, 0.051		1.510, 22.053	0.006, 0.032	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 37 of 264)

Biomarker: Cotinine ((ug/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.145, 0.073			0.120, 0.091		
	SD, SE	0.2624, 0.0618			0.0945, 0.0167		
	MEDIAN	0.073			0.098		
	MIN, MAX	0.008, 1.162			0.021, 0.390		
	5%, 95%	0.008, 1.162			0.026, 0.366		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.216, 0.073			0.118, 0.093		
	SD, SE	0.5939, 0.1400			0.0803, 0.0144		
	MEDIAN	0.070			0.095		
	MIN, MAX	0.005, 2.589			0.023, 0.336		
	5%, 95%	0.005, 2.589			0.025, 0.303		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.121, 0.084			0.127, 0.096		
	SD, SE	0.1159, 0.0281			0.1158, 0.0215		
	MEDIAN	0.106			0.096		
	MIN, MAX	0.002, 0.546			0.031, 0.580		
	5%, 95%	0.002, 0.546			0.035, 0.321		
	# of BLQ/ALQ Values	0/0			0/0		
Overall [*]	N	18		NA	32		NA
	MEAN, GEO MEAN	0.159, 0.080			0.124, 0.099		
	SD, SE	0.3206, 0.0756			0.0900, 0.0159		
	MEDIAN	0.087			0.105		
	MIN, MAX	0.005, 1.432			0.034, 0.435		
	5%, 95%	0.005, 1.432			0.035, 0.311		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 38 of 264)

Biomarker: Cotinine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.825, 0.415			0.679, 0.517		
	SD, SE	1.4884, 0.3508			0.5367, 0.0949		
	MEDIAN	0.411			0.554		
	MIN, MAX	0.047, 6.592			0.119, 2.215		
	5%, 95%	0.047, 6.592			0.149, 2.078		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1.223, 0.416			0.667, 0.527		
	SD, SE	3.3696, 0.7942			0.4562, 0.0819		
	MEDIAN	0.398			0.540		
	MIN, MAX	0.030, 14.690			0.129, 1.909		
	5%, 95%	0.030, 14.690			0.142, 1.721		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.688, 0.476			0.722, 0.546		
	SD, SE	0.6579, 0.1596			0.6568, 0.1220		
	MEDIAN	0.599			0.544		
	MIN, MAX	0.011, 3.099			0.177, 3.292		
	5%, 95%	0.011, 3.099			0.201, 1.821		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.904, 0.454			0.703, 0.563		
	SD, SE	1.8194, 0.4288			0.5114, 0.0904		
	MEDIAN	0.493			0.593		
	MIN, MAX	0.029, 8.127			0.190, 2.472		
	5%, 95%	0.029, 8.127			0.199, 1.767		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 39 of 264)

Biomarker: Cotinine (ng/mL)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1001.8, 749.5	2.3, 1.5		1044.9, 787.0	1.2, 1.1	
	SD, SE	574.80, 135.48	2.91, 0.53		650.99, 115.08	0.69, 0.12	
	MEDIAN	925.7	1.0		911.1	1.0	
	MIN, MAX	19.0, 2263.4	1.0, 14.1		18.2, 2626.8	1.0, 4.8	
	5%, 95%	19.0, 2263.4	1.0, 10.0		226.0, 2534.2	1.0, 2.2	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1183.3, 887.6	2.7, 1.6		1138.3, 880.3	1.2, 1.1	
	SD, SE	626.79, 147.74	4.14, 0.76		877.59, 157.62	0.40, 0.07	
	MEDIAN	1065.2	1.0		975.4	1.0	
	MIN, MAX	15.5, 2343.3	1.0, 20.8		81.5, 4778.6	1.0, 2.5	
	5%, 95%	15.5, 2343.3	1.0, 11.7		221.4, 2646.6	1.0, 2.4	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1107.1, 728.7	2.1, 1.4		1068.7, 908.3	1.1, 1.0	
	SD, SE	744.03, 180.45	3.49, 0.64		570.14, 105.87	0.46, 0.08	
	MEDIAN	844.3	1.0		1005.9	1.0	
	MIN, MAX	6.1, 2858.1	1.0, 19.9		121.1, 2580.2	1.0, 3.7	
	5%, 95%	6.1, 2858.1	1.0, 5.3		311.8, 2101.4	1.0, 1.2	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1101.6, 829.0	2.3, 1.6		1062.8, 856.8	1.1, 1.1	
	SD, SE	549.70, 129.57	2.96, 0.54		659.30, 116.55	0.42, 0.07	
	MEDIAN	1065.0	1.1		914.3	1.0	
	MIN, MAX	13.5, 1962.5	1.0, 13.9		73.6, 3090.2	1.0, 2.8	
	5%, 95%	13.5, 1962.5	1.0, 10.6		275.9, 2617.9	1.0, 2.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 40 of 264)

Biomarker: Cotinine (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5685.4, 4253.4	12.8, 8.8		5930.1, 4466.2	6.8, 6.3	
	SD, SE	3262.01, 768.86	16.53, 3.02		3694.37, 653.08	3.89, 0.66	
	MEDIAN	5253.1	5.7		5170.2	5.7	
	MIN, MAX	107.8, 12844.8	5.7, 80.0		103.3, 14907.1	5.7, 27.2	
	5%, 95%	107.8, 12844.8	5.7, 56.8		1282.6, 14381.6	5.7, 12.5	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	6715.1, 5037.2	15.3, 9.3		6459.7, 4995.6	6.6, 6.4	
	SD, SE	3557.04, 838.40	23.49, 4.29		4980.33, 894.49	2.24, 0.38	
	MEDIAN	6045.1	5.7		5535.4	5.7	
	MIN, MAX	88.0, 13298.2	5.7, 118.0		462.5, 27118.6	5.7, 14.2	
	5%, 95%	88.0, 13298.2	5.7, 66.4		1256.4, 15019.5	5.7, 13.6	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	6282.8, 4135.0	11.7, 8.0		6064.6, 5154.5	6.2, 6.0	
	SD, SE	4222.34, 1024.07	19.79, 3.61		3235.56, 600.83	2.59, 0.44	
	MEDIAN	4791.4	5.7		5708.5	5.7	
	MIN, MAX	34.6, 16219.7	5.7, 112.9		687.2, 14642.6	5.7, 21.0	
	5%, 95%	34.6, 16219.7	5.7, 30.1		1769.5, 11925.4	5.7, 6.8	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	6251.7, 4705.3	13.3, 9.2		6031.5, 4862.6	6.5, 6.3	
	SD, SE	3119.51, 735.28	16.80, 3.07		3741.56, 661.42	2.38, 0.40	
	MEDIAN	6043.6	6.4		5188.9	5.7	
	MIN, MAX	76.8, 11137.0	5.7, 78.7		417.7, 17537.1	5.7, 15.9	
	5%, 95%	76.8, 11137.0	5.7, 60.2		1566.0, 14856.4	5.7, 15.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 41 of 264)

Biomarker: Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	74.8, 59.1			74.2, 59.6		
	SD, SE	53.02, 12.50			52.55, 9.29		
	MEDIAN	59.0			58.2		
	MIN, MAX	6.3, 200.9			9.1, 262.7		
	5%, 95%	6.3, 200.9			15.1, 162.2		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	116.5, 70.3			87.7, 71.8		
	SD, SE	185.29, 43.67			61.81, 11.10		
	MEDIAN	72.0			67.8		
	MIN, MAX	5.2, 843.9			22.1, 294.1		
	5%, 95%	5.2, 843.9			30.9, 238.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	108.7, 68.5			80.3, 65.7		
	SD, SE	127.80, 31.00			61.09, 11.34		
	MEDIAN	68.5			62.0		
	MIN, MAX	2.0, 571.6			20.8, 322.5		
	5%, 95%	2.0, 571.6			29.5, 175.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	99.2, 68.4			80.5, 67.6		
	SD, SE	115.70, 27.27			54.54, 9.64		
	MEDIAN	65.7			63.1		
	MIN, MAX	4.5, 538.8			19.3, 293.1		
	5%, 95%	4.5, 538.8			31.8, 161.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	424.5, 335.2			421.2, 338.2		
	SD, SE	300.93, 70.93			298.22, 52.72		
	MEDIAN	334.6			330.1		
	MIN, MAX	35.9, 1140.3			51.7, 1490.7		
	5%, 95%	35.9, 1140.3			85.7, 920.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	661.1, 399.0			497.6, 407.4		
	SD, SE	1051.52, 247.85			350.77, 63.00		
	MEDIAN	408.4			385.0		
	MIN, MAX	29.3, 4789.2			125.6, 1668.8		
	5%, 95%	29.3, 4789.2			175.5, 1355.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	616.9, 388.9			455.8, 372.9		
	SD, SE	725.28, 175.91			346.75, 64.39		
	MEDIAN	388.5			352.1		
	MIN, MAX	11.5, 3243.9			118.0, 1830.3		
	5%, 95%	11.5, 3243.9			167.4, 993.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	562.7, 388.1			456.8, 383.6		
	SD, SE	656.63, 154.77			309.55, 54.72		
	MEDIAN	372.5			358.0		
	MIN, MAX	25.6, 3057.8			109.8, 1663.3		
	5%, 95%	25.6, 3057.8			180.6, 916.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	12775.686, 5928.173	12.447, NA		11946.851, 6284.199	3.616, NA	
	SD, SE	15906.0495, 3749.0918	24.9161, 4.5490		12768.6173, 2257.1940	7.5616, 1.2781	
	MEDIAN	6149.147	2.554		6802.623	0.000	
	MIN, MAX	71.505, 58435.475	0.000, 121.445		103.285, 57183.003	0.000, 31.780	
	5%, 95%	71.505, 58435.475	0.000, 49.373		193.518, 41739.058	0.000, 23.268	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	12429.228, 6666.938	14.169, NA		15118.109, 8074.155	4.232, NA	
	SD, SE	14017.9902, 3304.0720	24.9605, 4.5571		16526.0875, 2968.1729	7.1484, 1.2083	
	MEDIAN	8346.791	2.554		6741.333	0.000	
	MIN, MAX	73.775, 60546.008	0.000, 92.503		286.588, 77152.193	0.000, 24.970	
	5%, 95%	73.775, 60546.008	0.000, 71.505		310.423, 42263.995	0.000, 20.430	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	9575.361, 5758.281	8.929, NA		12155.165, 7318.112	2.659, NA	
	SD, SE	7119.6849, 1726.7772	16.0375, 2.9280		10191.6726, 1892.5461	6.5387, 1.1052	
	MEDIAN	8817.815	1.987		8595.355	0.000	
	MIN, MAX	81.153, 23770.305	0.000, 78.883		160.035, 37456.135	0.000, 28.943	
	5%, 95%	81.153, 23770.305	0.000, 36.320		900.623, 29846.528	0.000, 19.863	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	11720.704, 6790.708	11.848, NA		12733.509, 7363.967	3.502, NA	
	SD, SE	10966.1100, 2584.7369	18.0395, 3.2936		12218.3039, 2159.9114	6.1746, 1.0437	
	MEDIAN	9090.310	4.351		7428.198	0.568	
	MIN, MAX	75.478, 44996.319	0.000, 74.910		221.325, 53864.641	0.000, 23.268	
	5%, 95%	75.478, 44996.319	0.000, 52.400		430.165, 31626.019	0.000, 23.079	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate				
Timepoint	Statistic	Male			Female	
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers
Week 1	N	18		NA	32	NA
	MEAN, GEO MEAN	810.916, 467.157			734.934, 475.851	
	SD, SE	921.7349, 217.2550			688.4226, 121.6971	
	MEDIAN	456.287			586.977	
	MIN, MAX	23.835, 3712.490			51.643, 2599.227	
	5%, 95%	23.835, 3712.490			64.506, 2470.157	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	18		NA	31	NA
	MEAN, GEO MEAN	850.290, 528.079			1034.785, 658.445	
	SD, SE	723.5844, 170.5505			992.6234, 178.2804	
	MEDIAN	793.291			590.995	
	MIN, MAX	24.592, 2367.300			103.474, 3857.610	
	5%, 95%	24.592, 2367.300			126.571, 3761.075	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	17		NA	29	NA
	MEAN, GEO MEAN	949.137, 541.612			826.740, 529.423	
	SD, SE	1090.5024, 264.4857			717.1538, 133.1721	
	MEDIAN	533.582			606.714	
	MIN, MAX	27.051, 3961.718			32.007, 2846.864	
	5%, 95%	27.051, 3961.718			100.391, 2497.076	
	# of BLQ/ALQ Values	0/0			0/0	
Overall [*]	N	18		NA	32	NA
	MEAN, GEO MEAN	866.997, 562.016			862.992, 577.351	
	SD, SE	720.6777, 169.8654			745.8771, 131.8537	
	MEDIAN	667.112			698.097	
	MIN, MAX	25.159, 2522.024			66.662, 3026.032	
	5%, 95%	25.159, 2522.024			128.640, 2758.029	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	17099.631, 9702.851	18.077, NA		17856.776, 11002.526	7.214, NA	
	SD, SE	16437.8673, 3874.4425	31.1255, 5.6827		14914.8964, 2636.6061	17.8516, 3.0175	
	MEDIAN	14284.827	2.645		13051.204	0.000	
	MIN, MAX	100.822, 68661.683	0.000, 106.872		284.034, 60518.854	0.000, 75.621	
	5%, 95%	100.822, 68661.683	0.000, 106.084		561.202, 52173.823	0.000, 72.395	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	15578.821, 9437.531	23.010, NA		19694.105, 13152.196	8.773, NA	
	SD, SE	12680.2255, 2988.7578	43.7941, 7.9957		15548.2161, 2792.5421	15.3683, 2.5977	
	MEDIAN	14129.657	2.566		14973.828	0.000	
	MIN, MAX	66.398, 54491.407	0.000, 203.789		453.218, 68665.452	0.000, 54.934	
	5%, 95%	66.398, 54491.407	0.000, 103.001		523.023, 55851.960	0.000, 44.129	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	17262.737, 9735.883	15.560, NA		18129.673, 12558.609	5.147, NA	
	SD, SE	13557.2368, 3288.1129	27.1386, 4.9548		11936.9451, 2216.6351	13.0225, 2.2012	
	MEDIAN	14321.885	3.388		17400.969	0.000	
	MIN, MAX	85.048, 48342.568	0.000, 105.328		224.049, 48692.976	0.000, 52.637	
	5%, 95%	85.048, 48342.568	0.000, 102.548		1675.159, 37176.403	0.000, 50.216	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	16709.630, 10031.393	18.882, NA		18082.402, 12337.082	7.045, NA	
	SD, SE	13467.4893, 3174.3177	29.3085, 5.3510		13234.2559, 2339.5080	13.1343, 2.2201	
	MEDIAN	16733.542	4.780		15450.516	0.499	
	MIN, MAX	84.089, 57165.219	0.000, 104.966		412.823, 46589.501	0.000, 48.839	
	5%, 95%	84.089, 57165.219	0.000, 97.288		827.405, 46579.291	0.000, 42.815	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1093.850, 764.612			1145.880, 833.131		
	SD, SE	885.5225, 208.7197			1096.2961, 193.7996		
	MEDIAN	830.688			855.081		
	MIN, MAX	33.607, 3229.867			90.023, 6051.885		
	5%, 95%	33.607, 3229.867			142.017, 3069.048		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1075.089, 747.534			1451.953, 1072.558		
	SD, SE	811.5326, 191.2801			1335.1913, 239.8074		
	MEDIAN	860.829			1020.252		
	MIN, MAX	22.133, 3361.488			151.073, 6205.773		
	5%, 95%	22.133, 3361.488			443.000, 4389.603		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1362.232, 915.736			1216.198, 908.543		
	SD, SE	1000.7132, 242.7086			847.6669, 157.4078		
	MEDIAN	1273.684			995.011		
	MIN, MAX	28.349, 4080.569			44.810, 3246.198		
	5%, 95%	28.349, 4080.569			196.849, 3033.231		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	1169.703, 839.791			1268.057, 971.106		
	SD, SE	760.8145, 179.3257			1006.9520, 178.0057		
	MEDIAN	909.152			922.614		
	MIN, MAX	28.030, 2578.398			127.650, 5059.513		
	5%, 95%	28.030, 2578.398			276.448, 2748.884		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide (nmol/mg Creatinine) Analytical Lab: Harrogate

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	11.128, 7.340	0.011, NA		14.577, 9.395	0.006, NA	
	SD, SE	7.4252, 1.7501	0.0210, 0.0038		10.3373, 1.8274	0.0136, 0.0023	
	MEDIAN	10.682	0.002		14.598	0.000	
	MIN, MAX	0.095, 27.231	0.000, 0.075		0.236, 37.108	0.000, 0.055	
	5%, 95%	0.095, 27.231	0.000, 0.066		0.507, 36.704	0.000, 0.049	
	# of BLQ/ALQ Values	0/0	19/0		0/0	30/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	10.408, 6.935	0.016, NA		15.196, 10.444	0.007, NA	
	SD, SE	6.8410, 1.6124	0.0371, 0.0068		11.8468, 2.1277	0.0122, 0.0021	
	MEDIAN	10.268	0.002		13.259	0.000	
	MIN, MAX	0.074, 26.176	0.000, 0.195		0.392, 53.877	0.000, 0.045	
	5%, 95%	0.074, 26.176	0.000, 0.058		0.522, 38.730	0.000, 0.039	
	# of BLQ/ALQ Values	0/0	18/0		0/0	29/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	11.268, 7.027	0.008, NA		15.296, 10.711	0.005, NA	
	SD, SE	7.7146, 1.8711	0.0151, 0.0028		11.2894, 2.0964	0.0138, 0.0023	
	MEDIAN	9.472	0.002		14.211	0.000	
	MIN, MAX	0.075, 22.527	0.000, 0.060		0.264, 49.743	0.000, 0.067	
	5%, 95%	0.075, 22.527	0.000, 0.057		1.668, 40.962	0.000, 0.035	
	# of BLQ/ALQ Values	0/0	18/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	10.959, 7.253	0.012, NA		14.900, 10.481	0.006, NA	
	SD, SE	7.0907, 1.6713	0.0208, 0.0038		10.5712, 1.8687	0.0119, 0.0020	
	MEDIAN	11.094	0.002		14.601	0.000	
	MIN, MAX	0.081, 23.794	0.000, 0.091		0.388, 38.906	0.000, 0.049	
	5%, 95%	0.081, 23.794	0.000, 0.061		0.809, 38.799	0.000, 0.038	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Cotinine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)			Analytical Lab: Harrogate			
Timepoint	Statistic		Male		Female	
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers
Week 1	N	18		NA	32	NA
	MEAN, GEO MEAN	0.885, 0.579			0.918, 0.727	
	SD, SE	0.8592, 0.2025			0.6984, 0.1235	
	MEDIAN	0.503			0.761	
	MIN, MAX	0.032, 2.946			0.118, 3.670	
	5%, 95%	0.032, 2.946			0.169, 2.137	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	18		NA	31	NA
	MEAN, GEO MEAN	0.955, 0.550			1.108, 0.852	
	SD, SE	1.4836, 0.3497			0.9291, 0.1669	
	MEDIAN	0.550			0.839	
	MIN, MAX	0.025, 6.653			0.131, 4.303	
	5%, 95%	0.025, 6.653			0.403, 2.843	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	17		NA	29	NA
	MEAN, GEO MEAN	0.980, 0.661			1.069, 0.775	
	SD, SE	0.8366, 0.2029			1.0407, 0.1933	
	MEDIAN	0.722			0.772	
	MIN, MAX	0.025, 3.082			0.053, 5.120	
	5%, 95%	0.025, 3.082			0.209, 3.316	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	18		NA	32	NA
	MEAN, GEO MEAN	0.933, 0.611			1.044, 0.824	
	SD, SE	0.9816, 0.2314			0.8336, 0.1474	
	MEDIAN	0.617			0.830	
	MIN, MAX	0.027, 4.227			0.118, 4.364	
	5%, 95%	0.027, 4.227			0.325, 2.594	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (µg/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1685.189, 1137.843	7.867, 2.456		1778.702, 1034.077	2.202, 1.896	
	SD, SE	1101.8218, 259.7019	19.3657, 3.5357		1601.2984, 283.0722	1.5415, 0.2606	
	MEDIAN	1444.194	1.619		1281.883	1.900	
	MIN, MAX	18.048, 3521.714	0.530, 93.100		76.527, 5245.860	0.570, 9.792	
	5%, 95%	18.048, 3521.714	0.780, 58.311		83.814, 5088.650	0.800, 3.350	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1746.577, 1234.839	12.592, 2.332		1840.681, 1134.230	2.299, 2.000	
	SD, SE	992.7277, 233.9882	54.8383, 10.0121		1545.7478, 277.6245	1.4079, 0.2380	
	MEDIAN	1592.530	1.680		1490.076	2.150	
	MIN, MAX	10.980, 3494.785	0.625, 302.670		81.312, 5904.527	0.660, 8.514	
	5%, 95%	10.980, 3494.785	0.815, 12.512		94.792, 4764.320	0.750, 4.585	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2172.224, 1008.701	2.702, 2.114		1952.179, 1443.640	2.116, 1.974	
	SD, SE	2176.7037, 527.9282	2.5477, 0.4651		1234.0737, 229.1617	0.8139, 0.1376	
	MEDIAN	1269.580	1.900		1954.260	2.030	
	MIN, MAX	5.450, 6614.080	0.750, 13.650		55.800, 4262.175	0.940, 4.740	
	5%, 95%	5.450, 6614.080	0.750, 7.259		417.200, 4138.428	0.990, 3.350	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1878.760, 1253.987	7.721, 2.668		1799.419, 1211.436	2.206, 2.011	
	SD, SE	1166.6214, 274.9753	22.2784, 4.0675		1353.6781, 239.2987	0.9890, 0.1672	
	MEDIAN	1786.222	1.863		1574.517	2.150	
	MIN, MAX	11.493, 3792.219	0.793, 121.310		85.660, 4824.558	0.967, 5.165	
	5%, 95%	11.493, 3792.219	0.865, 33.074		130.092, 4299.995	0.980, 4.270	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	10389.190, 7014.802	48.501, 15.139		10965.699, 6375.083	13.578, 11.689	
	SD, SE	6792.7315, 1601.0622	119.3893, 21.7974		9872.0048, 1745.1404	9.5034, 1.6064	
	MEDIAN	8903.456	9.978		7902.809	11.714	
	MIN, MAX	111.266, 21711.367	3.267, 573.962		471.789, 32340.727	3.514, 60.368	
	5%, 95%	111.266, 21711.367	4.809, 359.487		516.713, 31371.527	4.932, 20.653	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	10767.648, 7612.786	77.631, 14.378		11347.798, 6992.529	14.176, 12.327	
	SD, SE	6120.1664, 1442.5371	338.0780, 61.7243		9529.5349, 1711.5550	8.6798, 1.4671	
	MEDIAN	9817.948	10.357		9186.319	13.255	
	MIN, MAX	67.692, 21545.350	3.853, 1865.961		501.288, 36401.409	4.069, 52.489	
	5%, 95%	67.692, 21545.350	5.024, 77.136		584.393, 29372.033	4.624, 28.267	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	13391.759, 6218.636	16.659, 13.035		12035.184, 8900.039	13.046, 12.167	
	SD, SE	13419.3783, 3254.6773	15.7067, 2.8676		7608.0647, 1412.7821	5.0180, 0.8482	
	MEDIAN	7826.961	11.714		12048.013	12.515	
	MIN, MAX	33.599, 40775.803	4.624, 84.152		344.007, 26276.309	5.795, 29.222	
	5%, 95%	33.599, 40775.803	4.624, 44.752		2572.038, 25513.409	6.103, 20.653	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	11582.557, 7730.816	47.597, 16.446		11093.418, 7468.500	13.600, 12.399	
	SD, SE	7192.2206, 1695.2226	137.3465, 25.0759		8345.4257, 1475.2768	6.0976, 1.0307	
	MEDIAN	11012.056	11.484		9706.899	13.255	
	MIN, MAX	70.852, 23379.028	4.891, 747.878		528.091, 29743.402	5.960, 31.832	
	5%, 95%	70.852, 23379.028	5.331, 203.904		802.015, 26509.469	6.042, 26.323	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ($\mu\text{g}/24\text{hr}/\text{cigarette per day}$) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	134.044, 89.665			107.059, 78.302		
	SD, SE	131.8900, 31.0868			82.0618, 14.5066		
	MEDIAN	114.896			86.057		
	MIN, MAX	6.016, 590.746			14.337, 363.475		
	5%, 95%	6.016, 590.746			16.763, 244.020		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	196.148, 97.810			129.311, 92.496		
	SD, SE	390.9936, 92.1581			102.5182, 18.4128		
	MEDIAN	100.419			85.370		
	MIN, MAX	3.660, 1747.393			16.262, 376.716		
	5%, 95%	3.660, 1747.393			16.394, 360.360		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	142.448, 94.877			131.410, 104.439		
	SD, SE	96.6999, 23.4532			87.7583, 16.2963		
	MEDIAN	145.831			107.140		
	MIN, MAX	1.817, 376.203			13.950, 422.898		
	5%, 95%	1.817, 376.203			29.233, 275.895		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^a	N	18		NA	32		NA
	MEAN, GEO MEAN	157.245, 104.761			119.177, 97.804		
	SD, SE	181.1319, 42.6932			75.5788, 13.3606		
	MEDIAN	121.480			96.236		
	MIN, MAX	3.831, 849.365			22.234, 287.989		
	5%, 95%	3.831, 849.365			40.787, 281.914		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 52 of 264)

Biomarker: Nicotine ((nmol/24hr/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	826.379, 552.787			660.019, 482.733		
	SD, SE	813.1014, 191.6498			505.9107, 89.4332		
	MEDIAN	708.333			530.544		
	MIN, MAX	37.089, 3641.947			88.388, 2240.823		
	5%, 95%	37.089, 3641.947			103.343, 1504.383		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1209.249, 602.998			797.203, 570.239		
	SD, SE	2410.4749, 568.1544			632.0241, 113.5149		
	MEDIAN	619.084			526.308		
	MIN, MAX	22.564, 10772.675			100.258, 2322.453		
	5%, 95%	22.564, 10772.675			101.072, 2221.619		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	878.195, 584.913			810.142, 643.866		
	SD, SE	596.1545, 144.5887			541.0306, 100.4669		
	MEDIAN	899.047			660.518		
	MIN, MAX	11.200, 2319.289			86.002, 2607.168		
	5%, 95%	11.200, 2319.289			180.219, 1700.894		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	969.418, 645.850			734.727, 602.959		
	SD, SE	1116.6774, 263.2034			465.9432, 82.3679		
	MEDIAN	748.925			593.294		
	MIN, MAX	23.618, 5236.332			137.071, 1775.452		
	5%, 95%	23.618, 5236.332			251.451, 1737.999		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 53 of 264)

Biomarker: Nicotine (µg/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.564, 0.861	0.005, NA		1.543, 0.902	0.002, NA	
	SD, SE	1.9898, 0.4690	0.0106, 0.0019		1.4185, 0.2508	0.0022, 0.0004	
	MEDIAN	1.038	0.001		1.072	0.002	
	MIN, MAX	0.017, 8.892	0.000, 0.044		0.050, 5.613	0.000, 0.014	
	5%, 95%	0.017, 8.892	0.000, 0.041		0.071, 5.001	0.001, 0.003	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1.463, 0.906	0.011, NA		1.458, 0.901	0.002, NA	
	SD, SE	1.5262, 0.3597	0.0525, 0.0096		1.3118, 0.2356	0.0014, 0.0002	
	MEDIAN	1.135	0.001		1.262	0.002	
	MIN, MAX	0.012, 6.916	0.000, 0.289		0.064, 5.630	0.000, 0.008	
	5%, 95%	0.012, 6.916	0.000, 0.014		0.071, 4.633	0.001, 0.004	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1.392, 0.730	0.001, NA		1.667, 1.232	0.002, 0.002	
	SD, SE	1.1591, 0.2811	0.0015, 0.0003		1.1687, 0.2170	0.0010, 0.0002	
	MEDIAN	1.218	0.001		1.493	0.002	
	MIN, MAX	0.005, 4.246	0.000, 0.008		0.056, 5.060	0.001, 0.005	
	5%, 95%	0.005, 4.246	0.000, 0.003		0.357, 4.177	0.001, 0.004	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.477, 0.920	0.006, NA		1.547, 1.032	0.002, NA	
	SD, SE	1.3164, 0.3103	0.0201, 0.0037		1.2482, 0.2207	0.0013, 0.0002	
	MEDIAN	1.237	0.001		1.362	0.002	
	MIN, MAX	0.011, 5.866	0.000, 0.111		0.061, 5.434	0.000, 0.007	
	5%, 95%	0.011, 5.866	0.000, 0.015		0.119, 4.066	0.001, 0.004	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 54 of 264)

Biomarker: Nicotine (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9.640, 5.307	0.028, NA		9.514, 5.558	0.012, NA	
	SD, SE	12.2671, 2.8914	0.0654, 0.0119		8.7453, 1.5460	0.0135, 0.0023	
	MEDIAN	6.396	0.006		6.606	0.012	
	MIN, MAX	0.105, 54.819	0.000, 0.271		0.308, 34.604	0.000, 0.086	
	5%, 95%	0.105, 54.819	0.000, 0.253		0.438, 30.831	0.006, 0.018	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	9.017, 5.588	0.070, NA		8.986, 5.553	0.012, NA	
	SD, SE	9.4091, 2.2178	0.3236, 0.0591		8.0873, 1.4525	0.0088, 0.0015	
	MEDIAN	6.994	0.006		7.780	0.012	
	MIN, MAX	0.074, 42.637	0.000, 1.782		0.395, 34.709	0.000, 0.049	
	5%, 95%	0.074, 42.637	0.000, 0.086		0.438, 28.562	0.006, 0.025	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	8.580, 4.502	0.009, NA		10.277, 7.593	0.012, 0.010	
	SD, SE	7.1459, 1.7331	0.0089, 0.0016		7.2053, 1.3380	0.0062, 0.0010	
	MEDIAN	7.509	0.006		9.204	0.012	
	MIN, MAX	0.031, 26.177	0.000, 0.049		0.345, 31.195	0.006, 0.031	
	5%, 95%	0.031, 26.177	0.000, 0.018		2.201, 25.751	0.006, 0.025	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall†	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9.107, 5.684	0.036, NA		9.537, 6.362	0.012, 0.010	
	SD, SE	8.1155, 1.9128	0.1234, 0.0225		7.6954, 1.3604	0.0073, 0.0012	
	MEDIAN	7.627	0.007		8.394	0.010	
	MIN, MAX	0.070, 36.164	0.000, 0.682		0.373, 33.503	0.002, 0.041	
	5%, 95%	0.070, 36.164	0.002, 0.094		0.734, 25.067	0.006, 0.025	

* P-value from Wilcoxon rank-sum test.

† Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.176, 0.068			0.091, 0.068		
	SD, SE	0.4043, 0.0953			0.0629, 0.0111		
	MEDIAN	0.074			0.069		
	MIN, MAX	0.006, 1.778			0.011, 0.251		
	5%, 95%	0.006, 1.778			0.014, 0.187		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.262, 0.072			0.102, 0.074		
	SD, SE	0.7989, 0.1883			0.0764, 0.0137		
	MEDIAN	0.062			0.065		
	MIN, MAX	0.004, 3.458			0.013, 0.250		
	5%, 95%	0.004, 3.458			0.013, 0.244		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.105, 0.070			0.112, 0.089		
	SD, SE	0.0828, 0.0201			0.0733, 0.0136		
	MEDIAN	0.094			0.090		
	MIN, MAX	0.002, 0.358			0.014, 0.287		
	5%, 95%	0.002, 0.358			0.028, 0.255		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.180, 0.078			0.101, 0.083		
	SD, SE	0.4224, 0.0996			0.0618, 0.0109		
	MEDIAN	0.081			0.079		
	MIN, MAX	0.004, 1.865			0.016, 0.228		
	5%, 95%	0.004, 1.865			0.027, 0.227		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 56 of 264)

Biomarker: Nicotine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1.084, 0.418			0.558, 0.421		
	SD, SE	2.4930, 0.5876			0.3876, 0.0685		
	MEDIAN	0.452			0.427		
	MIN, MAX	0.035, 10.964			0.067, 1.550		
	5%, 95%	0.035, 10.964			0.088, 1.153		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1.617, 0.443			0.628, 0.453		
	SD, SE	4.9253, 1.1609			0.4711, 0.0846		
	MEDIAN	0.382			0.401		
	MIN, MAX	0.025, 21.319			0.078, 1.541		
	5%, 95%	0.025, 21.319			0.079, 1.504		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.646, 0.423			0.692, 0.549		
	SD, SE	0.5108, 0.1239			0.4520, 0.0839		
	MEDIAN	0.581			0.557		
	MIN, MAX	0.010, 2.207			0.086, 1.771		
	5%, 95%	0.010, 2.207			0.171, 1.570		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	1.112, 0.477			0.624, 0.513		
	SD, SE	2.6039, 0.6138			0.3811, 0.0674		
	MEDIAN	0.500			0.490		
	MIN, MAX	0.023, 11.497			0.096, 1.408		
	5%, 95%	0.023, 11.497			0.169, 1.399		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine (ng/mL)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1071.6, 695.2	3.4, 1.7		1181.3, 590.6	1.2, 1.1	
	SD, SE	894.09, 210.74	6.00, 1.10		1369.23, 242.05	0.98, 0.17	
	MEDIAN	810.1	1.0		597.3	1.0	
	MIN, MAX	12.8, 3752.0	1.0, 24.5		32.7, 6329.6	1.0, 6.8	
	5%, 95%	12.8, 3752.0	1.0, 20.9		45.8, 3781.9	1.0, 1.2	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1278.9, 872.3	5.1, 1.5		1226.1, 696.3	1.1, 1.1	
	SD, SE	900.59, 212.27	19.15, 3.50		1429.99, 256.83	0.58, 0.10	
	MEDIAN	993.7	1.0		730.7	1.0	
	MIN, MAX	12.2, 3489.6	1.0, 106.2		67.2, 6634.3	1.0, 4.3	
	5%, 95%	12.2, 3489.6	1.0, 5.7		83.5, 4961.8	1.0, 2.1	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1075.5, 596.6	1.5, 1.2		1220.1, 841.2	1.0, 1.0	
	SD, SE	898.87, 218.01	1.80, 0.33		965.31, 179.25	0.07, 0.01	
	MEDIAN	820.2	1.0		1123.3	1.0	
	MIN, MAX	5.2, 3006.4	1.0, 10.5		30.0, 3630.2	1.0, 1.4	
	5%, 95%	5.2, 3006.4	1.0, 4.0		291.1, 3563.7	1.0, 1.0	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1160.2, 803.0	3.3, 1.6		1171.2, 714.3	1.1, 1.1	
	SD, SE	733.75, 172.95	7.75, 1.41		1158.40, 204.78	0.43, 0.07	
	MEDIAN	947.1	1.0		705.4	1.0	
	MIN, MAX	10.1, 2449.9	1.0, 42.7		65.6, 5531.4	1.0, 3.3	
	5%, 95%	10.1, 2449.9	1.0, 9.9		69.4, 3012.0	1.0, 2.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 58 of 264)

Biomarker: Nicotine (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	6606.6, 4285.8	20.9, 10.3		7282.7, 3641.2	7.3, 6.6	
	SD, SE	5512.07, 1299.21	36.96, 6.75		8441.30, 1492.23	6.03, 1.02	
	MEDIAN	4994.3	6.2		3682.4	6.2	
	MIN, MAX	78.9, 23131.1	6.2, 151.0		201.6, 39022.0	6.2, 41.9	
	5%, 95%	78.9, 23131.1	6.2, 128.8		282.4, 23315.4	6.2, 7.4	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	7884.4, 5377.8	31.2, 9.3		7559.2, 4292.7	7.0, 6.6	
	SD, SE	5552.14, 1308.65	118.03, 21.55		8815.87, 1583.38	3.58, 0.61	
	MEDIAN	6126.2	6.2		4504.8	6.2	
	MIN, MAX	75.2, 21513.4	6.2, 654.7		414.3, 40900.5	6.2, 26.5	
	5%, 95%	75.2, 21513.4	6.2, 35.1		514.8, 30589.5	6.2, 12.9	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	6630.4, 3678.3	9.3, 7.5		7522.2, 5186.3	6.3, 6.3	
	SD, SE	5541.54, 1344.02	11.07, 2.02		5951.14, 1105.10	0.41, 0.07	
	MEDIAN	5056.5	6.2		6925.1	6.2	
	MIN, MAX	32.1, 18534.5	6.2, 64.7		185.0, 22380.2	6.2, 8.6	
	5%, 95%	32.1, 18534.5	6.2, 24.7		1794.6, 21970.2	6.2, 6.2	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	7152.5, 4949.8	20.4, 10.2		7220.5, 4403.2	6.8, 6.6	
	SD, SE	4523.60, 1066.22	47.74, 8.72		7141.56, 1262.46	2.61, 0.44	
	MEDIAN	5838.7	6.3		4348.7	6.2	
	MIN, MAX	62.1, 15103.7	6.2, 263.2		404.2, 34100.9	6.2, 20.3	
	5%, 95%	62.1, 15103.7	6.2, 60.8		427.6, 18569.2	6.2, 13.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 59 of 264)

Biomarker: Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	85.3, 34.8			68.4, 44.7		
	SD, SE	88.05, 20.75			64.18, 11.35		
	MEDIAN	55.4			41.8		
	MIN, MAX	4.3, 312.7			8.1, 287.7		
	5%, 95%	4.3, 312.7			9.2, 189.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	142.9, 69.1			81.0, 56.8		
	SD, SE	257.04, 60.59			75.59, 13.58		
	MEDIAN	65.7			49.5		
	MIN, MAX	4.1, 1127.4			13.4, 331.7		
	5%, 95%	4.1, 1127.4			16.0, 236.3		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	87.1, 56.0			85.2, 60.9		
	SD, SE	86.17, 20.90			71.13, 13.21		
	MEDIAN	71.2			62.8		
	MIN, MAX	1.7, 374.9			7.5, 316.8		
	5%, 95%	1.7, 374.9			14.7, 242.0		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	105.2, 66.6			75.9, 57.5		
	SD, SE	133.46, 31.46			61.71, 10.91		
	MEDIAN	71.8			50.7		
	MIN, MAX	3.4, 603.3			14.5, 287.1		
	5%, 95%	3.4, 603.3			20.1, 209.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 60 of 264)

Biomarker: Nicotine ((nmol/L/cigarette per day) Analytical Lab: Harropate		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	525.5, 337.7			421.6, 275.7		
	SD, SE	542.84, 127.95			395.69, 69.95		
	MEDIAN	341.2			257.6		
	MIN, MAX	26.3, 1927.6			49.9, 1773.7		
	5%, 95%	26.3, 1927.6			56.5, 1165.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	880.7, 426.0			499.1, 350.1		
	SD, SE	1584.59, 373.49			465.96, 83.69		
	MEDIAN	404.6			305.0		
	MIN, MAX	25.1, 6950.1			82.9, 2045.0		
	5%, 95%	25.1, 6950.1			98.6, 1456.6		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	536.7, 346.0			525.1, 375.2		
	SD, SE	531.24, 128.84			438.50, 81.43		
	MEDIAN	438.7			387.3		
	MIN, MAX	10.7, 2311.4			46.3, 1952.9		
	5%, 95%	10.7, 2311.4			90.3, 1492.0		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	648.6, 410.4			467.9, 354.1		
	SD, SE	822.81, 193.94			380.53, 67.27		
	MEDIAN	442.3			312.3		
	MIN, MAX	20.7, 3719.4			89.0, 1770.2		
	5%, 95%	20.7, 3719.4			123.7, 1294.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 61 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	28	<.0001	31	34	<.0001
	MEAN, GEO MEAN	3185.833, 1315.053	3.369, NA		2857.657, 1385.609	0.526, NA	
	SD, SE	4046.7969, 953.8392	5.8234, 1.1005		3716.0670, 667.4253	1.5264, 0.2618	
	MEDIAN	1437.370	0.000		1405.004	0.000	
	MIN, MAX	17.879, 12968.078	0.000, 22.811		59.184, 17624.502	0.000, 6.782	
	5%, 95%	17.879, 12968.078	0.000, 18.495		71.514, 10892.322	0.000, 4.932	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	17	29	<.0001	31	34	<.0001
	MEAN, GEO MEAN	3220.379, 1984.938	5.166, NA		3586.081, 1633.399	0.399, NA	
	SD, SE	3208.1796, 778.0978	18.3997, 3.4167		4914.8761, 882.7378	1.7363, 0.2978	
	MEDIAN	1499.945	0.000		1458.639	0.000	
	MIN, MAX	330.444, 10055.115	0.000, 99.257		68.432, 25269.102	0.000, 9.864	
	5%, 95%	330.444, 10055.115	0.000, 11.714		106.038, 10255.478	0.000, 2.466	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	16	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2390.017, 1334.459	2.589, NA		3029.460, 1504.195	0.247, NA	
	SD, SE	1832.9412, 458.2353	5.7411, 1.0482		2699.1081, 501.2118	0.8745, 0.1478	
	MEDIAN	2286.599	0.000		2594.232	0.000	
	MIN, MAX	27.126, 5382.662	0.000, 28.976		12.330, 8494.754	0.000, 4.316	
	5%, 95%	27.126, 5382.662	0.000, 11.714		17.879, 8343.711	0.000, 2.466	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2837.219, 1507.004	3.689, NA		3047.122, 1633.131	0.393, NA	
	SD, SE	2855.8907, 673.1399	7.5385, 1.3763		3367.0203, 595.2107	1.1359, 0.1920	
	MEDIAN	1684.176	0.103		1332.873	0.000	
	MIN, MAX	22.503, 9135.914	0.000, 36.579		68.432, 14522.685	0.000, 5.549	
	5%, 95%	22.503, 9135.914	0.000, 19.112		98.640, 11621.847	0.000, 3.699	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 62 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	209.881, 103.631			172.883, 107.735		
	SD, SE	265.7647, 62.6413			203.3168, 36.5168		
	MEDIAN	99.003			113.411		
	MIN, MAX	5.960, 962.254			14.180, 1036.735		
	5%, 95%	5.960, 962.254			20.933, 495.106		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	17		NA	31		NA
	MEAN, GEO MEAN	225.933, 144.480			243.814, 133.203		
	SD, SE	209.2341, 50.7467			297.5609, 53.4435		
	MEDIAN	175.045			114.900		
	MIN, MAX	25.400, 730.384			4.562, 1263.455		
	5%, 95%	25.400, 730.384			39.086, 1139.498		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	16		NA	29		NA
	MEAN, GEO MEAN	220.431, 121.108			210.345, 108.820		
	SD, SE	211.2136, 52.8034			194.1911, 36.0604		
	MEDIAN	115.556			152.447		
	MIN, MAX	9.042, 626.981			1.192, 674.143		
	5%, 95%	9.042, 626.981			2.466, 555.261		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	209.357, 123.571			204.440, 130.280		
	SD, SE	199.7170, 47.0738			203.3880, 35.9543		
	MEDIAN	113.343			126.735		
	MIN, MAX	7.501, 705.631			22.263, 756.966		
	5%, 95%	7.501, 705.631			29.150, 750.779		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 63 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	28	<.0001	31	34	<.0001
	MEAN, GEO MEAN	4026.806, 2152.393	5.227, NA		4140.122, 2380.428	1.243, NA	
	SD, SE	3521.3809, 829.9974	8.9670, 1.6946		4418.1241, 793.5185	4.2370, 0.7266	
	MEDIAN	3048.346	0.000		2576.293	0.000	
	MIN, MAX	25.209, 10788.304	0.000, 29.594		162.756, 22030.628	0.000, 22.042	
	5%, 95%	25.209, 10788.304	0.000, 29.242		185.043, 11202.823	0.000, 11.235	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	17	29	<.0001	31	34	<.0001
	MEAN, GEO MEAN	4025.196, 2885.683	12.807, NA		4619.799, 2660.685	0.838, NA	
	SD, SE	3025.1895, 733.7162	52.2807, 9.7083		4867.0677, 874.1512	3.7823, 0.6487	
	MEDIAN	3547.286	0.000		3511.091	0.000	
	MIN, MAX	461.543, 9872.580	0.000, 282.882		177.318, 22489.501	0.000, 21.701	
	5%, 95%	461.543, 9872.580	0.000, 23.674		193.519, 16921.539	0.000, 4.389	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	16	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	4351.611, 2285.075	4.535, NA		4485.523, 2581.348	0.432, NA	
	SD, SE	3671.9016, 917.9754	8.5750, 1.5656		3249.7743, 603.4679	1.5813, 0.2673	
	MEDIAN	3945.803	0.000		4005.325	0.000	
	MIN, MAX	28.428, 11461.291	0.000, 37.669		17.262, 12487.288	0.000, 8.114	
	5%, 95%	28.428, 11461.291	0.000, 21.208		52.296, 10420.453	0.000, 4.279	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3965.133, 2293.944	7.466, NA		4289.753, 2765.078	0.839, NA	
	SD, SE	3288.3005, 775.0599	19.3413, 3.5312		3668.2894, 648.4681	2.6072, 0.4407	
	MEDIAN	3242.426	0.137		2982.790	0.000	
	MIN, MAX	26.819, 10353.310	0.000, 104.041		133.990, 15441.801	0.000, 11.885	
	5%, 95%	26.819, 10353.310	0.000, 21.634		199.791, 12852.562	0.000, 10.052	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 64 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	270.600, 169.615			263.934, 185.085		
	SD, SE	245.2307, 57.8014			277.0427, 49.7583		
	MEDIAN	178.233			183.997		
	MIN, MAX	8.403, 837.161			12.336, 1295.919		
	5%, 95%	8.403, 837.161			65.416, 1120.282		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	17		NA	31		NA
	MEAN, GEO MEAN	288.580, 210.043			345.767, 216.978		
	SD, SE	235.5505, 57.1294			409.8456, 73.6104		
	MEDIAN	236.486			193.519		
	MIN, MAX	59.810, 832.306			19.617, 1880.171		
	5%, 95%	59.810, 832.306			59.106, 1188.730		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	16		NA	29		NA
	MEAN, GEO MEAN	330.168, 207.380			310.569, 186.744		
	SD, SE	258.1362, 64.5341			251.8602, 46.7693		
	MEDIAN	298.331			246.060		
	MIN, MAX	9.476, 851.592			3.452, 929.600		
	5%, 95%	9.476, 851.592			3.486, 741.273		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	282.614, 190.149			302.153, 221.251		
	SD, SE	217.4618, 51.2562			271.8673, 48.0598		
	MEDIAN	168.425			193.557		
	MIN, MAX	8.940, 724.671			43.896, 1230.708		
	5%, 95%	8.940, 724.671			69.230, 908.341		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide (nmol/mg Creatinine) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	28	<.0001	31	34	<.0001
	MEAN, GEO MEAN	2.667, 1.629	0.003, NA		3.223, 2.054	0.001, NA	
	SD, SE	1.8782, 0.4427	0.0061, 0.0012		2.6290, 0.4722	0.0031, 0.0005	
	MEDIAN	2.644	0.000		3.131	0.000	
	MIN, MAX	0.024, 7.058	0.000, 0.023		0.135, 12.113	0.000, 0.016	
	5%, 95%	0.024, 7.058	0.000, 0.021		0.187, 7.068	0.000, 0.008	
	# of BLQ/ALQ Values	0/0	18/0		0/0	33/0	
Week 2	N	17	29	<.0001	31	34	<.0001
	MEAN, GEO MEAN	2.720, 2.069	0.011, NA		3.522, 2.113	0.001, NA	
	SD, SE	1.8726, 0.4542	0.0499, 0.0093		3.6051, 0.6475	0.0028, 0.0005	
	MEDIAN	2.323	0.000		2.864	0.000	
	MIN, MAX	0.298, 6.734	0.000, 0.270		0.153, 17.646	0.000, 0.016	
	5%, 95%	0.298, 6.734	0.000, 0.017		0.193, 11.734	0.000, 0.004	
	# of BLQ/ALQ Values	0/0	22/0		0/0	32/0	
Week 3	N	16	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2.776, 1.558	0.002, NA		3.701, 2.200	0.001, NA	
	SD, SE	2.1773, 0.5443	0.0045, 0.0008		2.7698, 0.5143	0.0018, 0.0003	
	MEDIAN	2.549	0.000		3.179	0.000	
	MIN, MAX	0.025, 6.372	0.000, 0.021		0.020, 10.645	0.000, 0.008	
	5%, 95%	0.025, 6.372	0.000, 0.011		0.056, 9.700	0.000, 0.006	
	# of BLQ/ALQ Values	0/0	23/0		0/0	34/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2.612, 1.659	0.006, NA		3.483, 2.345	0.001, NA	
	SD, SE	1.9175, 0.4520	0.0177, 0.0032		2.6610, 0.4704	0.0021, 0.0003	
	MEDIAN	2.521	0.000		2.952	0.000	
	MIN, MAX	0.025, 6.721	0.000, 0.097		0.120, 10.339	0.000, 0.009	
	5%, 95%	0.025, 6.721	0.000, 0.013		0.190, 9.409	0.000, 0.008	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate			
		Male		Female	
Timepoint	Statistic	Smokers	Non-Smokers	Smokers	Non-Smokers
Week 1	N	18		31	
	MEAN, GEO MEAN	0.216, 0.128		0.205, 0.160	
	SD, SE	0.2139, 0.0504		0.1622, 0.0291	
	MEDIAN	0.137		0.144	
	MIN, MAX	0.008, 0.684		0.031, 0.713	
	5%, 95%	0.008, 0.684		0.062, 0.679	
	# of BLQ/ALQ Values	0/0		0/0	
Week 2	N	17		31	
	MEAN, GEO MEAN	0.257, 0.151		0.259, 0.172	
	SD, SE	0.3877, 0.0940		0.2814, 0.0505	
	MEDIAN	0.123		0.165	
	MIN, MAX	0.043, 1.647		0.015, 1.304	
	5%, 95%	0.043, 1.647		0.051, 0.882	
	# of BLQ/ALQ Values	0/0		0/0	
Week 3	N	16		29	
	MEAN, GEO MEAN	0.226, 0.141		0.265, 0.160	
	SD, SE	0.1834, 0.0458		0.2669, 0.0496	
	MEDIAN	0.155		0.191	
	MIN, MAX	0.008, 0.531		0.004, 1.213	
	5%, 95%	0.008, 0.531		0.004, 0.888	
	# of BLQ/ALQ Values	0/0		0/0	
Overall*	N	18		32	
	MEAN, GEO MEAN	0.223, 0.138		0.245, 0.188	
	SD, SE	0.2319, 0.0547		0.2108, 0.0373	
	MEDIAN	0.127		0.194	
	MIN, MAX	0.008, 0.915		0.039, 1.065	
	5%, 95%	0.008, 0.915		0.091, 0.590	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 67 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	62.070, 44.228	0.095, NA		72.066, 53.384	0.053, 0.038	
	SD, SE	41.1904, 9.7087	0.1597, 0.0291		44.6144, 7.8868	0.0632, 0.0107	
	MEDIAN	54.596	0.033		66.924	0.033	
	MIN, MAX	0.762, 171.322	0.000, 0.677		1.870, 165.672	0.005, 0.340	
	5%, 95%	0.762, 171.322	0.016, 0.447		8.068, 162.785	0.017, 0.183	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	59.710, 41.943	0.178, NA		74.721, 57.970	0.056, 0.042	
	SD, SE	39.2615, 9.2540	0.5342, 0.0975		47.9812, 8.6177	0.0502, 0.0085	
	MEDIAN	50.999	0.038		64.581	0.033	
	MIN, MAX	0.520, 162.182	0.000, 2.938		5.674, 177.245	0.016, 0.243	
	5%, 95%	0.520, 162.182	0.011, 0.606		10.256, 175.663	0.017, 0.174	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	60.863, 40.299	0.064, 0.038		78.391, 62.940	0.051, 0.039	
	SD, SE	41.8253, 10.1441	0.0951, 0.0174		48.1753, 8.9459	0.0481, 0.0081	
	MEDIAN	51.737	0.030		63.710	0.033	
	MIN, MAX	0.402, 163.660	0.011, 0.470		10.306, 204.112	0.017, 0.283	
	5%, 95%	0.402, 163.660	0.016, 0.274		14.475, 177.849	0.017, 0.109	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	60.933, 43.007	0.113, 0.048		74.681, 58.662	0.053, 0.042	
	SD, SE	39.3367, 9.2717	0.2311, 0.0422		45.5234, 8.0475	0.0475, 0.0080	
	MEDIAN	58.041	0.034		66.336	0.039	
	MIN, MAX	0.561, 150.824	0.011, 1.222		5.950, 182.343	0.017, 0.236	
	5%, 95%	0.561, 150.824	0.013, 0.392		10.933, 163.962	0.017, 0.193	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	5.386, 3.485			4.725, 4.042		
	SD, SE	7.4367, 1.7528			2.9421, 0.5201		
	MEDIAN	3.417			3.973		
	MIN, MAX	0.254, 34.264			0.935, 14.783		
	5%, 95%	0.254, 34.264			1.986, 12.963		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	7.591, 3.322			5.495, 4.728		
	SD, SE	18.3926, 4.3352			3.2306, 0.5802		
	MEDIAN	3.239			4.715		
	MIN, MAX	0.173, 81.091			1.734, 15.686		
	5%, 95%	0.173, 81.091			2.051, 11.330		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	5.392, 3.790			5.287, 4.554		
	SD, SE	5.1386, 1.2463			3.6124, 0.6708		
	MEDIAN	4.092			4.413		
	MIN, MAX	0.134, 23.794			1.911, 20.287		
	5%, 95%	0.134, 23.794			2.024, 10.156		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	6.078, 3.610			5.238, 4.628		
	SD, SE	10.1725, 2.3977			2.9750, 0.5259		
	MEDIAN	3.583			4.388		
	MIN, MAX	0.187, 46.383			1.877, 16.312		
	5%, 95%	0.187, 46.383			2.556, 11.763		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	13.822, 9.484	0.026, 0.011		13.303, 9.931	0.010, 0.007	
	SD, SE	9.9619, 2.3460	0.0420, 0.0077		8.3518, 1.4764	0.0092, 0.0016	
	MEDIAN	13.406	0.006		12.589	0.008	
	MIN, MAX	0.131, 43.641	0.003, 0.157		0.365, 34.676	0.002, 0.039	
	5%, 95%	0.131, 43.641	0.003, 0.148		2.343, 27.701	0.003, 0.038	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	13.093, 9.255	0.039, 0.013		15.102, 11.844	0.011, 0.008	
	SD, SE	7.5570, 1.7812	0.0940, 0.0172		8.8042, 1.5813	0.0087, 0.0015	
	MEDIAN	13.281	0.009		14.179	0.007	
	MIN, MAX	0.075, 33.112	0.002, 0.499		0.923, 36.320	0.002, 0.032	
	5%, 95%	0.075, 33.112	0.003, 0.190		2.125, 33.028	0.003, 0.029	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	14.745, 9.058	0.020, 0.011		14.494, 11.972	0.009, 0.007	
	SD, SE	11.6886, 2.8349	0.0289, 0.0053		7.2037, 1.3377	0.0066, 0.0011	
	MEDIAN	11.316	0.008		14.750	0.007	
	MIN, MAX	0.074, 41.355	0.004, 0.136		1.679, 29.438	0.003, 0.035	
	5%, 95%	0.074, 41.355	0.004, 0.078		2.178, 24.083	0.003, 0.026	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	13.929, 9.603	0.028, 0.013		13.936, 11.167	0.010, 0.008	
	SD, SE	9.1277, 2.1514	0.0474, 0.0087		7.6523, 1.3527	0.0069, 0.0012	
	MEDIAN	11.551	0.010		14.050	0.008	
	MIN, MAX	0.093, 37.247	0.003, 0.222		0.989, 27.579	0.003, 0.030	
	5%, 95%	0.093, 37.247	0.004, 0.135		2.359, 27.575	0.003, 0.026	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/24hr/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.908, 0.748			0.892, 0.752		
	SD, SE	0.4563, 0.1076			0.6019, 0.1064		
	MEDIAN	0.800			0.777		
	MIN, MAX	0.044, 1.846			0.183, 3.468		
	5%, 95%	0.044, 1.846			0.273, 1.684		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1.109, 0.733			1.124, 0.966		
	SD, SE	1.4161, 0.3338			0.7293, 0.1310		
	MEDIAN	0.832			0.893		
	MIN, MAX	0.025, 6.647			0.425, 3.670		
	5%, 95%	0.025, 6.647			0.437, 2.761		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1.136, 0.853			0.957, 0.866		
	SD, SE	0.6417, 0.1556			0.4405, 0.0818		
	MEDIAN	1.085			0.881		
	MIN, MAX	0.025, 2.263			0.420, 2.007		
	5%, 95%	0.025, 2.263			0.429, 1.877		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	1.045, 0.802			0.988, 0.882		
	SD, SE	0.7335, 0.1729			0.5285, 0.0934		
	MEDIAN	0.890			0.955		
	MIN, MAX	0.031, 3.585			0.392, 3.005		
	5%, 95%	0.031, 3.585			0.424, 1.810		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/mg Creatinine) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	0.010, NA	0.000, NA		0.012, NA	0.000, NA	
	SD, SE	0.0068, 0.0016	0.0000, 0.0000		0.0073, 0.0013	0.0000, 0.0000	
	MEDIAN	0.009	0.000		0.011	0.000	
	MIN, MAX	0.000, 0.028	0.000, 0.000		0.000, 0.027	0.000, 0.000	
	5%, 95%	0.000, 0.028	0.000, 0.000		0.001, 0.026	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	0.010, NA	0.000, NA		0.012, 0.009	0.000, NA	
	SD, SE	0.0063, 0.0015	0.0000, 0.0000		0.0078, 0.0014	0.0000, 0.0000	
	MEDIAN	0.009	0.000		0.010	0.000	
	MIN, MAX	0.000, 0.026	0.000, 0.000		0.001, 0.029	0.000, 0.000	
	5%, 95%	0.000, 0.026	0.000, 0.000		0.002, 0.028	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	0.010, NA	0.000, NA		0.013, 0.010	0.000, NA	
	SD, SE	0.0068, 0.0017	0.0000, 0.0000		0.0078, 0.0014	0.0000, 0.0000	
	MEDIAN	0.008	0.000		0.010	0.000	
	MIN, MAX	0.000, 0.027	0.000, 0.000		0.002, 0.033	0.000, 0.000	
	5%, 95%	0.000, 0.027	0.000, 0.000		0.002, 0.029	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	0.010, NA	0.000, NA		0.012, 0.010	0.000, NA	
	SD, SE	0.0064, 0.0015	0.0000, 0.0000		0.0074, 0.0013	0.0000, 0.0000	
	MEDIAN	0.009	0.000		0.011	0.000	
	MIN, MAX	0.000, 0.024	0.000, 0.000		0.001, 0.030	0.000, 0.000	
	5%, 95%	0.000, 0.024	0.000, 0.000		0.002, 0.027	0.000, 0.000	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.001, NA			0.001, NA		
	SD, SE	0.0014, 0.0003			0.0006, 0.0001		
	MEDIAN	0.001			0.001		
	MIN, MAX	0.000, 0.006			0.000, 0.002		
	5%, 95%	0.000, 0.006			0.000, 0.002		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.001, NA			0.001, NA		
	SD, SE	0.0030, 0.0007			0.0007, 0.0001		
	MEDIAN	0.001			0.001		
	MIN, MAX	0.000, 0.013			0.000, 0.003		
	5%, 95%	0.000, 0.013			0.000, 0.002		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.001, NA			0.001, NA		
	SD, SE	0.0009, 0.0002			0.0007, 0.0001		
	MEDIAN	0.001			0.001		
	MIN, MAX	0.000, 0.004			0.000, 0.003		
	5%, 95%	0.000, 0.004			0.000, 0.002		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	0.001, NA			0.001, NA		
	SD, SE	0.0018, 0.0004			0.0007, 0.0001		
	MEDIAN	0.001			0.001		
	MIN, MAX	0.000, 0.008			0.000, 0.003		
	5%, 95%	0.000, 0.008			0.000, 0.002		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	85202.321, 58462.565	159.938, 67.755		82001.169, 61213.291	58.895, 44.579	
	SD, SE	61406.4097, 14473.6296	258.9385, 47.2755		51481.8797, 9100.7966	56.4888, 9.5484	
	MEDIAN	82633.120	37.278		77601.162	46.442	
	MIN, MAX	807.495, 269008.088	16.191, 965.245		2251.019, 213748.173	13.634, 237.553	
	5%, 95%	807.495, 269008.088	17.554, 910.691		14441.244, 170748.968	16.239, 234.212	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	80706.746, 57056.576	238.603, 79.085		93087.670, 73006.709	66.453, 50.878	
	SD, SE	46581.7789, 10979.4306	579.9512, 105.8841		54269.4223, 9747.0760	54.0386, 9.1342	
	MEDIAN	81866.447	55.334		87398.389	42.918	
	MIN, MAX	463.520, 204106.209	12.603, 3077.553		5691.880, 223877.537	14.343, 199.855	
	5%, 95%	463.520, 204106.209	15.682, 1170.521		13096.445, 203586.824	19.348, 176.749	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	90888.319, 55827.577	121.964, 68.946		89343.293, 73796.576	54.072, 44.842	
	SD, SE	72049.8950, 17474.6663	178.0699, 32.5110		44404.0636, 8245.6276	40.4937, 6.8447	
	MEDIAN	69754.394	48.161		90922.089	44.305	
	MIN, MAX	455.443, 254916.322	24.371, 838.565		10347.744, 181459.213	17.387, 214.464	
	5%, 95%	455.443, 254916.322	25.818, 479.785		13427.500, 148449.107	18.202, 161.224	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	85861.395, 59208.644	173.501, 79.279		85905.064, 68833.445	59.807, 49.004	
	SD, SE	56264.4210, 13261.6512	292.4969, 53.4024		47169.5124, 8338.4705	42.7707, 7.2296	
	MEDIAN	71198.076	56.633		86603.825	47.661	
	MIN, MAX	575.486, 229597.547	20.989, 1369.102		6096.881, 169998.026	16.995, 183.762	
	5%, 95%	575.486, 229597.547	21.248, 828.576		14539.033, 169972.601	20.862, 161.356	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/24hr/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	5597.160, 4607.020			5496.958, 4635.178		
	SD, SE	2813.1975, 663.0770			3710.2303, 655.8822		
	MEDIAN	4933.138			4786.547		
	MIN, MAX	269.165, 11381.236			1125.510, 21374.817		
	5%, 95%	269.165, 11381.236			1679.783, 10379.541		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	6832.907, 4519.371			6926.664, 5953.677		
	SD, SE	8729.3751, 2057.5334			4494.9220, 807.3118		
	MEDIAN	5129.101			5502.899		
	MIN, MAX	154.507, 40974.206			2619.289, 22620.758		
	5%, 95%	154.507, 40974.206			2696.009, 17016.199		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	7004.383, 5251.024			5899.075, 5338.755		
	SD, SE	3955.2792, 959.2961			2715.4895, 504.2537		
	MEDIAN	6687.793			5427.632		
	MIN, MAX	151.814, 13950.879			2586.936, 12370.759		
	5%, 95%	151.814, 13950.879			2642.015, 11572.851		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	6438.950, 4941.501			6088.668, 5435.886		
	SD, SE	4521.7761, 1065.7929			3257.9068, 575.9220		
	MEDIAN	5482.150			5888.948		
	MIN, MAX	191.829, 22102.107			2417.332, 18522.809		
	5%, 95%	191.829, 22102.107			2610.851, 11156.032		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 75 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	56466.8, 35719.0	92.9, 46.2		51422.5, 34962.7	31.8, 25.0	
	SD, SE	53151.00, 12527.81	158.41, 28.92		40492.71, 7158.17	31.63, 5.35	
	MEDIAN	39231.4	29.7		40087.7	17.6	
	MIN, MAX	572.7, 228943.1	17.1, 822.3		818.6, 185431.1	17.1, 165.0	
	5%, 95%	572.7, 228943.1	17.1, 346.0		5370.5, 117580.7	17.1, 116.9	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	60035.2, 40306.3	134.2, 50.9		64490.8, 44818.9	34.0, 27.3	
	SD, SE	49085.70, 11569.61	266.95, 48.74		54125.48, 9721.22	28.17, 4.76	
	MEDIAN	52177.3	31.1		48192.8	18.7	
	MIN, MAX	515.0, 226784.6	17.1, 1079.8		3118.8, 251547.8	17.1, 128.5	
	5%, 95%	515.0, 226784.6	17.1, 1035.9		10010.5, 175038.6	17.1, 112.3	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	49871.4, 33019.2	68.0, 39.3		55723.8, 43002.5	27.0, 23.0	
	SD, SE	34676.82, 8410.36	116.68, 21.30		37781.03, 7015.76	21.14, 3.57	
	MEDIAN	42119.1	28.9		47640.2	17.1	
	MIN, MAX	434.6, 124561.5	17.1, 645.0		5563.3, 161187.4	17.1, 123.5	
	5%, 95%	434.6, 124561.5	17.1, 163.5		9591.0, 129203.3	17.1, 60.8	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	56060.6, 39267.7	98.4, 50.7		55858.9, 41079.3	30.9, 26.1	
	SD, SE	38284.09, 9023.65	145.62, 26.59		40793.59, 7211.36	22.81, 3.86	
	MEDIAN	50201.9	38.5		43613.1	23.5	
	MIN, MAX	507.4, 175714.8	17.1, 555.8		3166.9, 177780.1	17.1, 110.3	
	5%, 95%	507.4, 175714.8	17.3, 482.6		8324.0, 129505.1	17.1, 100.4	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 76 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	3719.4, 2814.8			3348.5, 2647.4		
	SD, SE	2646.88, 623.88			2238.89, 395.78		
	MEDIAN	2775.4			2862.3		
	MIN, MAX	190.9, 10706.3			409.3, 8724.4		
	5%, 95%	190.9, 10706.3			879.4, 8428.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	5089.5, 3192.6			4614.6, 3655.0		
	SD, SE	5932.77, 1398.37			3421.37, 614.50		
	MEDIAN	3945.9			3777.3		
	MIN, MAX	171.7, 26435.0			1348.0, 13709.5		
	5%, 95%	171.7, 26435.0			1418.0, 13281.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	4966.7, 3105.8			3786.2, 3111.0		
	SD, SE	5840.25, 1416.47			2456.81, 456.22		
	MEDIAN	3429.6			2949.8		
	MIN, MAX	144.9, 24912.3			971.3, 11279.6		
	5%, 95%	144.9, 24912.3			1390.8, 7908.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	4572.0, 3243.8			3924.8, 3231.9		
	SD, SE	4155.78, 979.53			2526.51, 446.63		
	MEDIAN	3739.5			3502.5		
	MIN, MAX	169.2, 19091.7			1247.0, 11237.8		
	5%, 95%	169.2, 19091.7			1248.9, 9143.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Sum of Nicotine and Nicotine metabolites (mg/L) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9.2, 5.8	0.0, NA		8.4, 5.6	0.0, NA	
	SD, SE	8.61, 2.03	0.03, 0.00		6.57, 1.16	0.00, 0.00	
	MEDIAN	6.4	0.0		6.6	0.0	
	MIN, MAX	0.1, 37.1	0.0, 0.1		0.1, 30.1	0.0, 0.0	
	5%, 95%	0.1, 37.1	0.0, 0.1		0.9, 19.1	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	9.8, 6.6	0.0, NA		10.5, 7.3	0.0, NA	
	SD, SE	7.96, 1.88	0.05, 0.01		8.78, 1.58	0.00, 0.00	
	MEDIAN	8.5	0.0		7.8	0.0	
	MIN, MAX	0.1, 36.8	0.0, 0.2		0.5, 40.8	0.0, 0.0	
	5%, 95%	0.1, 36.8	0.0, 0.2		1.6, 28.4	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	8.1, 5.5	0.0, NA		9.0, 7.0	0.0, NA	
	SD, SE	5.63, 1.36	0.02, 0.00		6.12, 1.14	0.00, 0.00	
	MEDIAN	6.8	0.0		7.7	0.0	
	MIN, MAX	0.1, 20.2	0.0, 0.1		0.9, 26.1	0.0, 0.0	
	5%, 95%	0.1, 20.2	0.0, 0.0		1.6, 21.0	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9.1, 6.5	0.0, NA		9.1, 6.7	0.0, NA	
	SD, SE	6.21, 1.46	0.03, 0.01		6.62, 1.17	0.00, 0.00	
	MEDIAN	8.2	0.0		7.1	0.0	
	MIN, MAX	0.1, 28.5	0.0, 0.1		0.5, 28.8	0.0, 0.0	
	5%, 95%	0.1, 28.5	0.0, 0.1		1.4, 21.0	0.0, 0.0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 78 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.6, NA			0.5, 0.4		
	SD, SE	0.43, 0.10			0.36, 0.06		
	MEDIAN	0.5			0.5		
	MIN, MAX	0.0, 1.7			0.1, 1.4		
	5%, 95%	0.0, 1.7			0.1, 1.4		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.8, NA			0.7, 0.6		
	SD, SE	0.97, 0.23			0.56, 0.10		
	MEDIAN	0.7			0.6		
	MIN, MAX	0.0, 4.3			0.2, 2.2		
	5%, 95%	0.0, 4.3			0.2, 2.2		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.8, NA			0.6, 0.5		
	SD, SE	0.94, 0.23			0.39, 0.07		
	MEDIAN	0.6			0.5		
	MIN, MAX	0.0, 4.0			0.2, 1.8		
	5%, 95%	0.0, 4.0			0.2, 1.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.7, NA			0.6, 0.5		
	SD, SE	0.67, 0.16			0.41, 0.07		
	MEDIAN	0.7			0.6		
	MIN, MAX	0.0, 3.1			0.2, 1.8		
	5%, 95%	0.0, 3.1			0.2, 1.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 79 of 264)

Biomarker: Total 3-hydroxycotinine (µg/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	8481.670, 5058.786	12.639, 5.259		7465.196, 5530.506	4.663, 3.147	
	SD, SE	7495.7959, 1766.7760	19.7909, 3.6133		5073.8646, 896.9410	5.5203, 0.9331	
	MEDIAN	7795.655	3.555		7094.738	2.800	
	MIN, MAX	80.370, 31233.615	0.950, 84.568		185.625, 21231.840	0.800, 25.920	
	5%, 95%	80.370, 31233.615	1.030, 59.985		1264.620, 17386.180	1.140, 19.728	
	# of BLQ/ALQ Values	0/0	8/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	7771.087, 5070.702	18.479, 6.526		9033.252, 6974.017	5.648, 3.680	
	SD, SE	5217.2058, 1229.7072	36.8337, 6.7249		5553.5372, 997.4447	6.3066, 1.0660	
	MEDIAN	7298.235	3.674		8284.165	2.795	
	MIN, MAX	48.420, 20994.570	1.000, 191.422		504.248, 22147.192	1.050, 24.208	
	5%, 95%	48.420, 20994.570	1.023, 74.670		1171.885, 19677.560	1.240, 23.013	
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	8564.710, 4903.589	12.223, 5.533		8436.228, 6644.598	4.361, 3.162	
	SD, SE	7430.9813, 1802.2777	20.2196, 3.6916		5351.4056, 993.7311	4.4083, 0.7451	
	MEDIAN	6563.699	3.665		7278.863	2.870	
	MIN, MAX	52.295, 27454.900	1.430, 89.830		1258.180, 19074.831	1.068, 21.688	
	5%, 95%	52.295, 27454.900	1.720, 55.313		1308.324, 17880.045	1.089, 14.840	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	8308.200, 5267.651	14.447, 6.474		8107.255, 6415.476	4.891, 3.558	
	SD, SE	6258.3618, 1475.1100	22.2395, 4.0604		5035.7608, 890.2051	4.5939, 0.7765	
	MEDIAN	6721.081	5.076		7035.315	2.883	
	MIN, MAX	60.362, 23472.750	1.318, 97.065		666.066, 20817.954	1.067, 20.305	
	5%, 95%	60.362, 23472.750	1.374, 66.991		1386.126, 16456.732	1.303, 18.212	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/24hr) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	44130.128, 26320.861	65.762, 27.363		38841.414, 28775.223	24.263, 16.373	
	SD, SE	39000.6263, 9192.5358	102.9721, 18.8001		26399.3178, 4666.7842	28.7220, 4.8549	
	MEDIAN	40560.793	18.497		36913.920	14.568	
	MIN, MAX	418.165, 162508.499	4.943, 440.007		965.807, 110469.264	4.162, 134.862	
	5%, 95%	418.165, 162508.499	5.359, 312.102		6579.818, 90460.295	5.931, 102.645	
Week 2	# of BLQ/ALQ Values	0/0	8/0	<.0001	0/0	15/0	<.0001
	N	18	30		31	35	
	MEAN, GEO MEAN	40432.968, 26382.858	96.144, 33.953		47000.013, 36285.812	29.385, 19.145	
	SD, SE	27145.1218, 6398.1666	191.6461, 34.9896		28895.0539, 5189.7049	32.8133, 5.5465	
	MEDIAN	37972.717	19.113		43102.510	14.542	
	MIN, MAX	251.929, 109234.748	5.203, 995.969		2623.602, 115231.840	5.463, 125.954	
Week 3	5%, 95%	251.929, 109234.748	5.323, 388.508	<.0001	6097.318, 102382.345	6.452, 119.737	<.0001
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
	N	17	30		29	35	
	MEAN, GEO MEAN	44562.185, 25513.374	63.595, 28.790		43893.696, 34571.846	22.692, 16.452	
	SD, SE	38663.3961, 9377.2509	105.2024, 19.2072		27843.3632, 5170.3827	22.9362, 3.8769	
	MEDIAN	34150.926	19.069		37871.924	14.933	
Overall ^b	MIN, MAX	272.091, 142847.845	7.440, 467.385	<.0001	6546.311, 99246.346	5.557, 112.843	<.0001
	5%, 95%	272.091, 142847.845	8.949, 287.794		6807.210, 93029.874	5.666, 77.213	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
	N	18	30		32	35	
	MEAN, GEO MEAN	43227.562, 27407.581	75.167, 33.685		42182.049, 33379.721	25.447, 18.511	
	SD, SE	32562.2568, 7674.9975	115.7120, 21.1260		26201.0638, 4631.7375	23.9026, 4.0403	
Overall ^b	MEDIAN	34969.785	26.410	<.0001	36604.744	15.002	<.0001
	MIN, MAX	314.062, 122128.717	6.859, 505.029		3465.540, 108315.817	5.550, 105.649	
	5%, 95%	314.062, 122128.717	7.151, 348.552		7212.012, 85624.375	6.778, 94.757	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 81 of 264)

Biomarker: Total 3-hydroxycotinine ((ug/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	518.293, 398.647			514.451, 418.780		
	SD, SE	265.0141, 62.4644			361.5090, 63.9064		
	MEDIAN	497.403			411.498		
	MIN, MAX	26.790, 1041.121			92.813, 1738.618		
	5%, 95%	26.790, 1041.121			148.548, 1220.408		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	632.378, 401.643			674.091, 568.729		
	SD, SE	761.0430, 179.3796			426.5924, 76.6183		
	MEDIAN	500.314			535.339		
	MIN, MAX	16.140, 3571.898			226.150, 1837.330		
	5%, 95%	16.140, 3571.898			234.377, 1632.510		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	686.349, 461.222			537.154, 480.698		
	SD, SE	480.7707, 116.6040			277.6903, 51.5658		
	MEDIAN	606.335			478.038		
	MIN, MAX	17.432, 1676.349			222.522, 1418.901		
	5%, 95%	17.432, 1676.349			224.937, 1089.147		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	608.687, 437.008			577.776, 504.000		
	SD, SE	432.0203, 101.8282			326.0893, 57.6450		
	MEDIAN	539.388			481.105		
	MIN, MAX	20.121, 2030.196			199.073, 1516.938		
	5%, 95%	20.121, 2030.196			215.772, 1303.658		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 82 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	2696.680, 2074.160			2676.690, 2178.910		
	SD, SE	1378.8686, 325.0025			1880.9313, 332.5048		
	MEDIAN	2587.989			2141.025		
	MIN, MAX	139.388, 5416.950			482.904, 9046.030		
	5%, 95%	139.388, 5416.950			772.896, 6349.783		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	3290.262, 2089.748			3507.296, 2959.098		
	SD, SE	3959.7063, 933.3117			2219.5603, 398.6448		
	MEDIAN	2603.135			2785.367		
	MIN, MAX	83.976, 18584.583			1176.658, 9559.628		
	5%, 95%	83.976, 18584.583			1219.464, 8493.950		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	3571.073, 2399.735			2794.814, 2501.073		
	SD, SE	2501.4498, 606.6907			1444.8224, 268.2968		
	MEDIAN	3154.763			2487.232		
	MIN, MAX	90.697, 8722.043			1157.784, 7382.540		
	5%, 95%	90.697, 8722.043			1170.349, 5666.830		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	3166.997, 2273.752			3006.160, 2622.312		
	SD, SE	2247.8017, 529.8119			1696.6422, 299.9268		
	MEDIAN	2806.435			2503.186		
	MIN, MAX	104.687, 10563.111			1035.779, 7892.630		
	5%, 95%	104.687, 10563.111			1122.662, 6782.931		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 83 of 264)

Biomarker: Total 3-hydroxycotinine (ug/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5.847, 3.827	0.008, NA		6.788, 4.823	0.004, 0.003	
	SD, SE	4.1160, 0.9701	0.0122, 0.0022		4.9747, 0.8794	0.0069, 0.0012	
	MEDIAN	5.353	0.002		5.406	0.002	
	MIN, MAX	0.076, 15.997	0.000, 0.052		0.154, 18.383	0.001, 0.037	
	5%, 95%	0.076, 15.997	0.001, 0.042		0.676, 18.231	0.001, 0.022	
	# of BLQ/ALQ Values	0/0	8/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	5.688, 3.726	0.011, NA		7.402, 5.538	0.005, 0.003	
	SD, SE	4.0901, 0.9640	0.0217, 0.0040		5.3130, 0.9542	0.0060, 0.0010	
	MEDIAN	4.759	0.004		5.898	0.002	
	MIN, MAX	0.054, 15.619	0.000, 0.099		0.503, 20.024	0.001, 0.027	
	5%, 95%	0.054, 15.619	0.001, 0.071		0.918, 18.908	0.001, 0.021	
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	5.880, 3.539	0.006, 0.003		7.537, 5.667	0.004, 0.003	
	SD, SE	4.7052, 1.1412	0.0104, 0.0019		5.6364, 1.0466	0.0050, 0.0008	
	MEDIAN	5.037	0.002		4.992	0.002	
	MIN, MAX	0.046, 17.626	0.001, 0.050		1.148, 23.294	0.001, 0.029	
	5%, 95%	0.046, 17.626	0.001, 0.026		1.303, 17.524	0.001, 0.010	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5.814, 3.797	0.008, 0.004		7.186, 5.455	0.004, 0.003	
	SD, SE	4.1774, 0.9846	0.0125, 0.0023		5.1148, 0.9042	0.0053, 0.0009	
	MEDIAN	4.913	0.003		5.573	0.002	
	MIN, MAX	0.059, 16.414	0.001, 0.046		0.653, 20.195	0.001, 0.026	
	5%, 95%	0.059, 16.414	0.001, 0.039		0.914, 17.186	0.001, 0.021	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 84 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	30.420, 19.913	0.039, NA		35.319, 25.093	0.023, 0.014	
	SD, SE	21.4154, 5.0476	0.0638, 0.0116		25.8835, 4.5756	0.0358, 0.0061	
	MEDIAN	27.849	0.010		28.128	0.010	
	MIN, MAX	0.395, 83.232	0.000, 0.271		0.801, 95.647	0.005, 0.193	
	5%, 95%	0.395, 83.232	0.005, 0.219		3.517, 94.856	0.005, 0.114	
	# of BLQ/ALQ Values	0/0	8/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	29.593, 19.388	0.059, NA		38.511, 28.813	0.025, 0.015	
	SD, SE	21.2809, 5.0160	0.1128, 0.0206		27.6433, 4.9649	0.0314, 0.0053	
	MEDIAN	24.761	0.019		30.687	0.010	
	MIN, MAX	0.281, 81.266	0.000, 0.515		2.617, 104.185	0.005, 0.140	
	5%, 95%	0.281, 81.266	0.005, 0.369		4.776, 98.378	0.005, 0.109	
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	30.593, 18.410	0.032, 0.015		39.214, 29.486	0.021, 0.014	
	SD, SE	24.4813, 5.9376	0.0541, 0.0099		29.3260, 5.4457	0.0262, 0.0044	
	MEDIAN	26.208	0.010		25.973	0.010	
	MIN, MAX	0.239, 91.708	0.005, 0.260		5.973, 121.199	0.005, 0.151	
	5%, 95%	0.239, 91.708	0.005, 0.135		6.780, 91.177	0.005, 0.052	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	30.249, 19.747	0.043, 0.020		37.388, 28.380	0.023, 0.016	
	SD, SE	21.7351, 5.1230	0.0652, 0.0119		26.6119, 4.7044	0.0275, 0.0046	
	MEDIAN	25.563	0.016		28.996	0.012	
	MIN, MAX	0.305, 85.402	0.003, 0.241		3.399, 105.075	0.005, 0.135	
	5%, 95%	0.305, 85.402	0.005, 0.203		4.755, 89.417	0.005, 0.111	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 85 of 264)

Biomarker: Total 3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.457, 0.302			0.457, 0.365		
	SD, SE	0.5352, 0.1261			0.3435, 0.0607		
	MEDIAN	0.373			0.377		
	MIN, MAX	0.021, 2.536			0.077, 1.823		
	5%, 95%	0.021, 2.536			0.161, 1.054		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.683, 0.295			0.545, 0.452		
	SD, SE	1.5982, 0.3767			0.3337, 0.0599		
	MEDIAN	0.342			0.479		
	MIN, MAX	0.018, 7.069			0.139, 1.274		
	5%, 95%	0.018, 7.069			0.171, 1.211		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.551, 0.333			0.488, 0.410		
	SD, SE	0.6392, 0.1550			0.3344, 0.0621		
	MEDIAN	0.420			0.326		
	MIN, MAX	0.015, 2.859			0.151, 1.709		
	5%, 95%	0.015, 2.859			0.186, 1.165		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.559, 0.317			0.505, 0.428		
	SD, SE	0.9084, 0.2141			0.3106, 0.0549		
	MEDIAN	0.392			0.435		
	MIN, MAX	0.019, 4.155			0.163, 1.389		
	5%, 95%	0.019, 4.155			0.187, 1.346		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	2.376, 1.569			2.376, 1.900		
	SD, SE	2.7846, 0.6563			1.7873, 0.3160		
	MEDIAN	1.940			1.960		
	MIN, MAX	0.107, 13.195			0.401, 9.486		
	5%, 95%	0.107, 13.195			0.839, 5.486		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	3.552, 1.536			2.833, 2.350		
	SD, SE	8.3151, 1.9599			1.7359, 0.3118		
	MEDIAN	1.780			2.490		
	MIN, MAX	0.094, 36.780			0.725, 6.629		
	5%, 95%	0.094, 36.780			0.890, 6.299		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2.865, 1.732			2.538, 2.133		
	SD, SE	3.3257, 0.8066			1.7400, 0.3231		
	MEDIAN	2.184			1.695		
	MIN, MAX	0.080, 14.876			0.786, 8.891		
	5%, 95%	0.080, 14.876			0.969, 6.061		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	2.907, 1.649			2.625, 2.227		
	SD, SE	4.7263, 1.1140			1.6155, 0.2856		
	MEDIAN	2.037			2.263		
	MIN, MAX	0.102, 21.617			0.850, 7.227		
	5%, 95%	0.102, 21.617			0.974, 7.002		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 87 of 264)

Biomarker: Total 3-hydroxycotinine (ng/mL)		Analytical Lab: Harrogate					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5422.5, 3090.8	8.4, 3.6		4520.5, 3158.8	2.7, 1.8	
	SD, SE	6007.04, 1415.87	17.48, 3.19		3406.88, 602.26	3.64, 0.62	
	MEDIAN	3942.6	3.2		3835.6	1.1	
	MIN, MAX	57.0, 26581.8	1.0, 96.1		67.5, 15165.6	1.0, 18.0	
	5%, 95%	57.0, 26581.8	1.0, 21.5		547.1, 12291.4	1.0, 14.4	
	# of BLQ/ALQ Values	0/0	8/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	5759.2, 3582.1	13.2, 4.2		6105.6, 4281.4	3.0, 2.0	
	SD, SE	5203.34, 1226.44	31.84, 5.81		4702.90, 844.67	3.77, 0.64	
	MEDIAN	4781.9	2.7		4802.7	1.3	
	MIN, MAX	53.8, 23327.3	1.0, 169.4		276.3, 16335.0	1.0, 17.5	
	5%, 95%	53.8, 23327.3	1.0, 57.6		968.5, 16284.7	1.0, 13.6	
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	4831.2, 2900.2	6.8, 3.1		5180.2, 3871.9	2.2, 1.6	
	SD, SE	3990.41, 967.82	12.95, 2.36		4458.33, 827.89	2.40, 0.41	
	MEDIAN	4218.2	2.5		3922.3	1.0	
	MIN, MAX	49.9, 14967.4	1.0, 69.1		703.4, 23404.7	1.0, 12.5	
	5%, 95%	49.9, 14967.4	1.0, 21.9		898.7, 11352.7	1.0, 6.9	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5401.5, 3535.5	9.5, 4.2		5159.8, 3843.3	2.7, 1.9	
	SD, SE	4129.77, 973.40	16.09, 2.94		3827.67, 676.64	2.76, 0.47	
	MEDIAN	5004.8	3.5		3829.5	1.3	
	MIN, MAX	53.6, 18644.1	1.0, 66.3		349.1, 18285.0	1.0, 12.3	
	5%, 95%	53.6, 18644.1	1.0, 61.9		835.5, 11100.3	1.0, 11.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 88 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/L)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	28213.3, 16081.4	43.9, 18.6		23520.0, 16435.2	13.9, 9.2	
	SD, SE	31254.64, 7366.79	90.93, 16.60		17726.02, 3133.55	18.94, 3.20	
	MEDIAN	20513.4	16.7		19956.6	5.7	
	MIN, MAX	296.6, 138305.1	5.2, 500.0		351.2, 78906.6	5.2, 93.7	
	5%, 95%	296.6, 138305.1	5.2, 111.9		2846.6, 63952.2	5.2, 74.9	
	# of BLQ/ALQ Values	0/0	8/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	29965.1, 18637.5	68.6, 21.8		31767.7, 22275.9	15.9, 10.3	
	SD, SE	27072.96, 6381.16	165.69, 30.25		24469.20, 4394.80	19.64, 3.32	
	MEDIAN	24880.2	14.1		24988.4	6.8	
	MIN, MAX	279.9, 121371.9	5.2, 881.4		1437.6, 84991.0	5.2, 91.1	
	5%, 95%	279.9, 121371.9	5.2, 299.7		5039.1, 84729.3	5.2, 70.8	
	# of BLQ/ALQ Values	0/0	2/0		0/0	13/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	25136.6, 15089.8	35.6, 16.4		26952.4, 20145.6	11.6, 8.4	
	SD, SE	20762.11, 5035.55	67.36, 12.30		23196.68, 4307.52	12.50, 2.11	
	MEDIAN	21947.3	12.8		20407.7	5.2	
	MIN, MAX	259.6, 77875.4	5.2, 359.5		3659.8, 121774.7	5.2, 65.0	
	5%, 95%	259.6, 77875.4	5.2, 113.9		4675.9, 59068.1	5.2, 35.9	
	# of BLQ/ALQ Values	0/0	7/0		0/0	18/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	28104.0, 18394.8	49.4, 22.0		26846.2, 19996.4	13.8, 9.9	
	SD, SE	21487.20, 5064.58	83.69, 15.28		19915.37, 3520.57	14.36, 2.43	
	MEDIAN	26040.0	18.2		19924.9	6.8	
	MIN, MAX	278.7, 97005.2	5.2, 344.8		1816.2, 95136.9	5.2, 64.0	
	5%, 95%	278.7, 97005.2	5.4, 322.2		4347.1, 57754.9	5.2, 58.8	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	336.1, 243.6			308.3, 239.2		
	SD, SE	236.01, 55.63			222.79, 39.38		
	MEDIAN	306.9			240.2		
	MIN, MAX	19.0, 886.1			33.8, 824.6		
	5%, 95%	19.0, 886.1			67.7, 794.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	477.4, 283.7			449.6, 349.1		
	SD, SE	543.13, 128.02			366.34, 65.80		
	MEDIAN	367.5			361.8		
	MIN, MAX	17.9, 2304.5			113.1, 1898.5		
	5%, 95%	17.9, 2304.5			124.6, 1113.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	510.7, 272.8			339.8, 280.1		
	SD, SE	703.82, 170.70			238.87, 44.36		
	MEDIAN	319.2			239.8		
	MIN, MAX	16.6, 2993.5			94.8, 1017.6		
	5%, 95%	16.6, 2993.5			122.3, 950.2		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	439.2, 290.4			371.6, 300.9		
	SD, SE	421.42, 99.33			266.90, 47.18		
	MEDIAN	379.5			284.2		
	MIN, MAX	17.8, 1912.2			104.8, 1253.8		
	5%, 95%	17.8, 1912.2			118.2, 924.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 90 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1748.6, 1267.3			1604.1, 1244.5		
	SD, SE	1227.94, 289.43			1159.16, 204.91		
	MEDIAN	1596.7			1249.7		
	MIN, MAX	98.9, 4610.2			175.6, 4290.4		
	5%, 95%	98.9, 4610.2			352.3, 4135.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2484.1, 1476.3			2339.4, 1816.6		
	SD, SE	2825.84, 666.06			1906.12, 342.35		
	MEDIAN	1912.0			1882.5		
	MIN, MAX	93.3, 11990.1			588.3, 9878.0		
	5%, 95%	93.3, 11990.1			648.0, 5793.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2657.0, 1419.3			1768.2, 1457.4		
	SD, SE	3661.97, 888.16			1242.87, 230.79		
	MEDIAN	1661.0			1247.7		
	MIN, MAX	86.5, 15575.1			493.0, 5294.6		
	5%, 95%	86.5, 15575.1			636.1, 4943.7		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2285.1, 1511.3			1933.4, 1565.3		
	SD, SE	2192.66, 516.81			1388.68, 245.49		
	MEDIAN	1974.4			1478.7		
	MIN, MAX	92.9, 9949.3			545.2, 6523.5		
	5%, 95%	92.9, 9949.3			614.7, 4809.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 91 of 264)

Biomarker: Total Cotinine (ug/24hr) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4697.127, 3151.036	7.373, 3.378		4980.328, 3583.251	3.560, 2.536	
	SD, SE	3405.8661, 802.7703	10.9875, 2.0060		3510.2690, 620.5337	4.1082, 0.6944	
	MEDIAN	4337.910	1.985		4470.819	2.565	
	MIN, MAX	44.556, 14394.338	0.950, 46.593		100.100, 17099.775	0.570, 20.150	
	5%, 95%	44.556, 14394.338	1.030, 31.240		720.720, 10349.625	0.800, 16.174	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	4529.454, 3076.865	9.251, 3.780		5307.500, 4056.020	3.933, 2.847	
	SD, SE	2787.8435, 657.1010	17.8779, 3.2640		3484.5950, 625.8517	3.5793, 0.6050	
	MEDIAN	4738.128	3.046		5108.532	2.480	
	MIN, MAX	25.650, 11710.980	0.625, 95.190		240.900, 16352.593	0.750, 13.755	
	5%, 95%	25.650, 11710.980	0.820, 27.225		735.694, 14208.645	0.915, 12.760	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	5082.502, 3029.686	6.551, 3.654		5097.602, 4137.160	3.155, 2.484	
	SD, SE	3857.0403, 935.4697	9.7076, 1.7724		2623.3481, 487.1435	2.9360, 0.4963	
	MEDIAN	3803.840	2.654		5222.565	2.395	
	MIN, MAX	21.379, 13322.126	1.350, 43.940		520.428, 10294.830	0.990, 15.268	
	5%, 95%	21.379, 13322.126	1.430, 33.930		756.280, 9606.210	1.034, 11.925	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4774.447, 3201.346	7.725, 3.939		5005.216, 3905.527	3.549, 2.768	
	SD, SE	3149.1211, 742.2550	11.0103, 2.0102		2989.8478, 528.5354	2.9976, 0.5067	
	MEDIAN	4549.285	2.795		5168.867	2.632	
	MIN, MAX	30.528, 13142.481	1.133, 48.539		287.143, 12691.083	0.967, 11.705	
	5%, 95%	30.528, 13142.481	1.193, 30.177		834.401, 10962.570	1.167, 11.541	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	26656.198, 17882.131	41.839, 19.170		28263.359, 20334.948	20.202, 14.390	
	SD, SE	19328.2899, 4555.7216	62.3538, 11.3842		19920.7764, 3521.5290	23.3141, 3.9408	
	MEDIAN	24617.640	11.265		25371.898	14.556	
	MIN, MAX	252.855, 81687.868	5.391, 264.415		568.068, 97041.223	3.235, 114.351	
	5%, 95%	252.855, 81687.868	5.845, 177.287		4090.086, 58734.122	4.540, 91.787	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	25704.650, 17461.209	52.500, 21.453		30120.061, 23017.914	22.322, 16.155	
	SD, SE	15821.0119, 3729.0483	101.4570, 18.5234		19775.0765, 3551.7086	20.3127, 3.4335	
	MEDIAN	26888.877	17.286		28990.919	14.074	
	MIN, MAX	145.564, 66459.812	3.547, 540.203		1367.108, 92800.965	4.256, 78.060	
	5%, 95%	145.564, 66459.812	4.654, 154.502		4175.063, 80634.060	5.193, 72.413	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	28843.196, 17193.472	37.175, 20.737		28928.891, 23478.382	17.902, 14.098	
	SD, SE	21888.7039, 5308.7905	55.0906, 10.0581		14887.5004, 2764.5394	16.6615, 2.8163	
	MEDIAN	21586.792	15.062		29638.056	13.592	
	MIN, MAX	121.326, 75603.065	7.661, 249.360		2953.429, 58423.160	5.618, 86.646	
	5%, 95%	121.326, 75603.065	8.115, 192.553		4291.889, 54515.242	5.868, 67.674	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	27094.985, 18167.650	43.838, 22.354		28404.604, 22163.866	20.142, 15.706	
	SD, SE	17871.2622, 4212.2969	62.4834, 11.4079		16967.3859, 2999.4384	17.0113, 2.8754	
	MEDIAN	25817.193	15.859		29333.321	14.935	
	MIN, MAX	173.248, 74583.582	6.432, 275.461		1629.535, 72021.894	5.486, 66.424	
	5%, 95%	173.248, 74583.582	6.772, 171.255		4735.227, 62212.586	6.621, 65.497	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 93 of 264)

Biomarker: Total Cotinine ((μ g/24hr/cigarette per day))		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	317.798, 248.311			336.076, 271.330		
	SD, SE	202.3497, 47.6943			284.6036, 50.3113		
	MEDIAN	257.105			290.369		
	MIN, MAX	14.852, 761.880			50.050, 1709.978		
	5%, 95%	14.852, 761.880			67.906, 608.801		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	363.151, 243.714			401.127, 330.767		
	SD, SE	406.4886, 95.8103			316.2812, 56.8058		
	MEDIAN	273.776			299.705		
	MIN, MAX	8.550, 1900.378			154.802, 1578.738		
	5%, 95%	8.550, 1900.378			168.956, 1113.879		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	395.614, 284.965			349.524, 299.300		
	SD, SE	238.6764, 57.8875			205.2411, 38.1123		
	MEDIAN	397.482			266.882		
	MIN, MAX	7.126, 918.949			104.652, 870.428		
	5%, 95%	7.126, 918.949			130.107, 845.604		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	356.143, 267.708			360.842, 307.890		
	SD, SE	237.1620, 55.8996			244.4457, 43.2123		
	MEDIAN	280.147			273.036		
	MIN, MAX	10.176, 1032.382			123.497, 1378.107		
	5%, 95%	10.176, 1032.382			140.352, 735.186		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1803.502, 1409.164			1907.232, 1539.798		
	SD, SE	1148.3342, 270.6650			1615.1252, 285.5165		
	MEDIAN	1459.071			1647.840		
	MIN, MAX	84.285, 4323.669			284.034, 9704.122		
	5%, 95%	84.285, 4323.669			385.369, 3454.948		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2060.879, 1383.077			2276.398, 1877.105		
	SD, SE	2306.8222, 543.7232			1794.8960, 322.3728		
	MEDIAN	1553.675			1700.826		
	MIN, MAX	48.521, 10784.643			878.503, 8959.340		
	5%, 95%	48.521, 10784.643			958.827, 6321.264		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2245.111, 1617.182			1983.549, 1698.525		
	SD, SE	1354.4876, 328.5115			1164.7429, 216.2873		
	MEDIAN	2255.712			1514.553		
	MIN, MAX	40.442, 5215.035			593.900, 4939.676		
	5%, 95%	40.442, 5215.035			738.357, 4798.800		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2021.113, 1519.244			2047.778, 1747.273		
	SD, SE	1345.8940, 317.2302			1387.2286, 245.2297		
	MEDIAN	1589.832			1549.477		
	MIN, MAX	57.749, 5858.764			700.849, 7820.754		
	5%, 95%	57.749, 5858.764			796.500, 4172.178		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (µg/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3.409, 2.384	0.005, NA		4.265, 3.125	0.003, NA	
	SD, SE	2.1337, 0.5029	0.0074, 0.0014		2.5826, 0.4565	0.0036, 0.0006	
	MEDIAN	3.233	0.001		4.284	0.002	
	MIN, MAX	0.042, 8.403	0.000, 0.033		0.083, 10.371	0.000, 0.015	
	5%, 95%	0.042, 8.403	0.001, 0.021		0.473, 8.958	0.001, 0.014	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	3.265, 2.263	0.007, NA		4.176, 3.220	0.003, 0.002	
	SD, SE	1.9738, 0.4652	0.0164, 0.0030		2.7789, 0.4991	0.0031, 0.0005	
	MEDIAN	2.968	0.002		3.723	0.002	
	MIN, MAX	0.029, 7.522	0.000, 0.091		0.240, 12.831	0.001, 0.015	
	5%, 95%	0.029, 7.522	0.001, 0.015		0.635, 9.853	0.001, 0.009	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	3.363, 2.188	0.004, 0.002		4.440, 3.529	0.003, 0.002	
	SD, SE	2.1802, 0.5288	0.0054, 0.0010		2.7980, 0.5196	0.0035, 0.0006	
	MEDIAN	2.961	0.002		3.807	0.002	
	MIN, MAX	0.019, 7.284	0.001, 0.025		0.518, 11.859	0.001, 0.020	
	5%, 95%	0.019, 7.284	0.001, 0.019		0.832, 10.517	0.001, 0.008	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3.344, 2.331	0.005, 0.002		4.291, 3.340	0.003, 0.002	
	SD, SE	2.0124, 0.4743	0.0083, 0.0015		2.6178, 0.4628	0.0030, 0.0005	
	MEDIAN	3.191	0.002		3.974	0.002	
	MIN, MAX	0.030, 7.123	0.001, 0.042		0.280, 10.694	0.001, 0.015	
	5%, 95%	0.030, 7.123	0.001, 0.018		0.733, 8.923	0.001, 0.010	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	19.343, 13.527	0.026, NA		24.206, 17.733	0.018, NA	
	SD, SE	12.1086, 2.8540	0.0420, 0.0077		14.6561, 2.5908	0.0202, 0.0034	
	MEDIAN	18.345	0.006		24.309	0.011	
	MIN, MAX	0.238, 47.687	0.000, 0.187		0.471, 58.855	0.000, 0.085	
	5%, 95%	0.238, 47.687	0.006, 0.119		2.684, 50.837	0.006, 0.079	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	18.530, 12.843	0.038, NA		23.701, 18.276	0.019, 0.014	
	SD, SE	11.2015, 2.6402	0.0932, 0.0170		15.7703, 2.8324	0.0173, 0.0029	
	MEDIAN	16.841	0.009		21.128	0.011	
	MIN, MAX	0.165, 42.687	0.000, 0.516		1.362, 72.816	0.006, 0.085	
	5%, 95%	0.165, 42.687	0.006, 0.085		3.609, 55.916	0.006, 0.051	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	19.086, 12.417	0.021, 0.012		25.199, 20.024	0.017, 0.013	
	SD, SE	12.3729, 3.0009	0.0306, 0.0056		15.8784, 2.9485	0.0196, 0.0033	
	MEDIAN	16.804	0.011		21.605	0.011	
	MIN, MAX	0.108, 41.337	0.006, 0.142		2.940, 67.300	0.006, 0.114	
	5%, 95%	0.108, 41.337	0.006, 0.108		4.722, 59.684	0.006, 0.045	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	18.974, 13.230	0.028, 0.014		24.354, 18.957	0.018, 0.014	
	SD, SE	11.4205, 2.6918	0.0475, 0.0087		14.8558, 2.6262	0.0170, 0.0029	
	MEDIAN	18.107	0.010		22.550	0.011	
	MIN, MAX	0.170, 40.425	0.004, 0.240		1.591, 60.690	0.004, 0.085	
	5%, 95%	0.170, 40.425	0.004, 0.104		4.162, 50.636	0.006, 0.057	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234^a will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.301, 0.188			0.281, 0.237		
	SD, SE	0.3833, 0.0904			0.1893, 0.0335		
	MEDIAN	0.159			0.232		
	MIN, MAX	0.014, 1.681			0.042, 1.037		
	5%, 95%	0.014, 1.681			0.098, 0.690		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.384, 0.180			0.313, 0.263		
	SD, SE	0.8490, 0.2001			0.2209, 0.0397		
	MEDIAN	0.178			0.242		
	MIN, MAX	0.010, 3.761			0.113, 1.095		
	5%, 95%	0.010, 3.761			0.123, 0.716		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.294, 0.205			0.316, 0.255		
	SD, SE	0.2489, 0.0604			0.2777, 0.0516		
	MEDIAN	0.199			0.233		
	MIN, MAX	0.006, 1.089			0.080, 1.482		
	5%, 95%	0.006, 1.089			0.120, 0.831		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.324, 0.196			0.308, 0.263		
	SD, SE	0.4792, 0.1129			0.2129, 0.0376		
	MEDIAN	0.194			0.241		
	MIN, MAX	0.010, 2.177			0.104, 1.205		
	5%, 95%	0.010, 2.177			0.111, 0.584		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1.710, 1.066			1.597, 1.343		
	SD, SE	2.1745, 0.5125			1.0751, 0.1900		
	MEDIAN	0.903			1.311		
	MIN, MAX	0.079, 9.537			0.236, 5.886		
	5%, 95%	0.079, 9.537			0.555, 3.918		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2.178, 1.017			1.775, 1.490		
	SD, SE	4.8185, 1.1357			1.2531, 0.2251		
	MEDIAN	1.011			1.374		
	MIN, MAX	0.055, 21.344			0.639, 6.213		
	5%, 95%	0.055, 21.344			0.700, 4.063		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1.668, 1.168			1.791, 1.449		
	SD, SE	1.4125, 0.3426			1.5764, 0.2927		
	MEDIAN	1.129			1.321		
	MIN, MAX	0.036, 6.180			0.455, 8.413		
	5%, 95%	0.036, 6.180			0.680, 4.718		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	1.837, 1.113			1.747, 1.493		
	SD, SE	2.7193, 0.6409			1.2081, 0.2136		
	MEDIAN	1.101			1.368		
	MIN, MAX	0.057, 12.354			0.588, 6.837		
	5%, 95%	0.057, 12.354			0.628, 3.315		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 99 of 264)

Biomarker: Total Cotinine (ng/mL) Analytical Lab: Harrogate		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3253.1, 1925.2	4.5, 2.3		3150.1, 2046.6	1.8, 1.4	
	SD, SE	3277.32, 772.47	7.06, 1.29		2736.60, 483.77	1.77, 0.30	
	MEDIAN	1979.1	1.5		2234.6	1.0	
	MIN, MAX	31.6, 12250.5	1.0, 35.5		36.4, 12610.5	1.0, 7.1	
	5%, 95%	31.6, 12250.5	1.0, 16.7		348.7, 8279.7	1.0, 6.7	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	3373.5, 2173.6	5.2, 2.4		3802.3, 2490.0	1.9, 1.5	
	SD, SE	2964.30, 698.69	7.93, 1.45		3672.50, 659.60	1.52, 0.26	
	MEDIAN	2387.9	1.5		2731.6	1.0	
	MIN, MAX	28.5, 13012.2	1.0, 33.4		132.0, 18373.7	1.0, 5.8	
	5%, 95%	28.5, 13012.2	1.0, 23.2		503.9, 9222.8	1.0, 5.5	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2794.4, 1791.9	3.6, 2.1		3210.5, 2410.8	1.6, 1.3	
	SD, SE	1879.15, 455.76	6.18, 1.13		2211.83, 410.73	1.52, 0.26	
	MEDIAN	2377.4	1.4		2429.1	1.0	
	MIN, MAX	20.4, 5701.3	1.0, 33.8		279.8, 7919.1	1.0, 8.8	
	5%, 95%	20.4, 5701.3	1.0, 11.7		540.2, 7304.4	1.0, 4.5	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3167.0, 2117.4	4.4, 2.5		3306.6, 2322.6	1.8, 1.5	
	SD, SE	2358.10, 555.81	5.89, 1.07		2691.91, 475.87	1.40, 0.24	
	MEDIAN	3091.3	1.8		2198.6	1.1	
	MIN, MAX	26.8, 9891.3	1.0, 27.1		149.4, 12581.8	1.0, 6.9	
	5%, 95%	26.8, 9891.3	1.0, 17.1		464.3, 7394.7	1.0, 5.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/L) Analytical Lab: Harrogate

Timepoint	Statistic	Smokers	Male Non-Smokers	P-value*	Smokers	Female Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	18461.1, 10925.4	25.3, 13.1		17876.9, 11614.6	10.4, 8.1	
	SD, SE	18598.78, 4383.78	40.09, 7.32		15530.19, 2745.38	10.06, 1.70	
	MEDIAN	11231.4	8.3		12681.1	5.7	
	MIN, MAX	179.3, 69521.6	5.7, 201.5		206.6, 71564.6	5.7, 40.3	
	5%, 95%	179.3, 69521.6	5.7, 94.8		1978.9, 46987.3	5.7, 38.0	
	# of BLQ/ALQ Values	0/0	11/0		0/0	22/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	19144.4, 12334.9	29.5, 13.8		21577.8, 14130.7	10.8, 8.7	
	SD, SE	16822.38, 3965.07	44.99, 8.21		20841.45, 3743.24	8.63, 1.46	
	MEDIAN	13551.4	8.5		15501.8	5.7	
	MIN, MAX	161.7, 73844.2	5.7, 189.5		749.1, 104270.7	5.7, 32.9	
	5%, 95%	161.7, 73844.2	5.7, 131.7		2859.6, 52339.4	5.7, 31.2	
	# of BLQ/ALQ Values	0/0	12/0		0/0	20/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	15858.2, 10169.2	20.6, 11.8		18219.8, 13681.3	8.9, 7.2	
	SD, SE	10664.18, 2586.44	35.06, 6.40		12552.13, 2330.87	8.63, 1.46	
	MEDIAN	13491.7	7.7		13785.1	5.7	
	MIN, MAX	115.8, 32354.9	5.7, 191.8		1587.9, 44940.9	5.7, 49.9	
	5%, 95%	115.8, 32354.9	5.7, 66.4		3065.6, 41452.5	5.7, 25.5	
	# of BLQ/ALQ Values	0/0	14/0		0/0	25/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	17972.4, 12017.3	25.1, 14.2		18765.0, 13180.7	10.0, 8.3	
	SD, SE	13382.22, 3154.22	33.38, 6.09		15276.63, 2700.55	7.89, 1.33	
	MEDIAN	17543.0	10.3		12476.8	6.3	
	MIN, MAX	152.3, 56133.3	5.7, 153.6		847.9, 71401.7	5.7, 39.0	
	5%, 95%	152.3, 56133.3	5.7, 97.2		2634.7, 41965.1	5.7, 31.0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	217.7, 151.7			203.7, 155.0		
	SD, SE	198.77, 46.85			156.49, 27.66		
	MEDIAN	130.3			162.6		
	MIN, MAX	10.5, 842.8			18.2, 698.0		
	5%, 95%	10.5, 842.8			56.1, 573.2		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	266.3, 172.2			270.0, 203.1		
	SD, SE	278.90, 65.74			224.22, 40.27		
	MEDIAN	205.0			191.9		
	MIN, MAX	9.5, 1226.1			55.3, 956.8		
	5%, 95%	9.5, 1226.1			57.9, 918.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	276.0, 168.6			226.0, 174.4		
	SD, SE	301.66, 73.16			174.19, 32.35		
	MEDIAN	156.9			181.7		
	MIN, MAX	6.8, 1140.3			38.5, 824.2		
	5%, 95%	6.8, 1140.3			61.5, 527.9		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	251.9, 175.2			232.6, 182.4		
	SD, SE	217.21, 51.20			173.34, 30.64		
	MEDIAN	176.0			191.7		
	MIN, MAX	8.9, 885.7			50.8, 826.3		
	5%, 95%	8.9, 885.7			58.7, 647.5		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 102 of 264)

Biomarker: Total Cotinine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value*	Smokers	Female Non-Smokers	P-value*
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1235.4, 861.0			1156.2, 879.5		
	SD, SE	1128.04, 265.88			888.06, 156.99		
	MEDIAN	739.1			922.9		
	MIN, MAX	59.8, 4782.9			103.3, 3960.9		
	5%, 95%	59.8, 4782.9			318.3, 3252.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1511.4, 977.0			1532.3, 1152.4		
	SD, SE	1582.72, 373.05			1272.44, 228.54		
	MEDIAN	1163.4			1088.8		
	MIN, MAX	53.9, 6957.9			313.8, 5429.9		
	5%, 95%	53.9, 6957.9			328.4, 5213.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1566.0, 956.5			1282.5, 989.8		
	SD, SE	1711.90, 415.20			988.55, 183.57		
	MEDIAN	890.5			1031.3		
	MIN, MAX	38.6, 6471.0			218.3, 4677.2		
	5%, 95%	38.6, 6471.0			349.2, 2996.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	1429.7, 994.6			1319.8, 1035.0		
	SD, SE	1232.61, 290.53			983.70, 173.89		
	MEDIAN	998.8			1088.0		
	MIN, MAX	50.8, 5026.3			288.3, 4689.3		
	5%, 95%	50.8, 5026.3			333.1, 3674.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 103 of 264)

Biomarker: Total Nicotine (ug/24hr) Analytical Lab: Harrogate

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2338.361, 1614.224	8.489, 2.808		2416.285, 1539.707	2.341, 1.999	
	SD, SE	1411.7402, 332.7504	19.1396, 3.4944		1963.9919, 347.1880	1.5130, 0.2558	
	MEDIAN	2319.819	2.018		1879.747	1.980	
	MIN, MAX	22.137, 4893.750	0.530, 88.160		116.325, 6337.875	0.570, 7.776	
	5%, 95%	22.137, 4893.750	0.650, 63.054		152.361, 6081.580	0.800, 6.825	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	2363.200, 1645.412	14.592, 2.585		2590.040, 1722.630	2.392, 2.059	
	SD, SE	1282.6174, 302.3158	63.1483, 11.5293		2121.2380, 380.9856	1.4247, 0.2408	
	MEDIAN	2157.762	1.680		2081.685	2.160	
	MIN, MAX	10.710, 4608.540	0.625, 348.555		150.672, 9552.459	0.660, 7.128	
	5%, 95%	10.710, 4608.540	0.815, 14.926		192.780, 5988.015	0.750, 6.160	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	2835.837, 1478.693	3.438, 2.468		2679.758, 2063.144	2.186, 2.031	
	SD, SE	2590.2593, 628.2302	3.7708, 0.6885		1574.9807, 292.4666	0.8578, 0.1450	
	MEDIAN	1851.270	2.125		2397.850	2.050	
	MIN, MAX	10.061, 7734.320	0.750, 19.760		95.232, 5749.170	0.940, 4.740	
	5%, 95%	10.061, 7734.320	0.750, 8.410		420.000, 5508.024	0.990, 3.948	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	2520.494, 1688.989	8.840, 3.003		2484.738, 1756.542	2.306, 2.088	
	SD, SE	1535.5364, 361.9294	25.2248, 4.6054		1748.7958, 309.1463	1.0526, 0.1779	
	MEDIAN	2405.250	1.953		1934.386	2.150	
	MIN, MAX	14.303, 5334.185	0.977, 138.186		162.499, 6909.321	0.967, 4.729	
	5%, 95%	14.303, 5334.185	1.057, 32.968		172.571, 5294.825	0.980, 4.724	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 104 of 264)

Biomarker: Total Nicotine (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	14415.995, 9951.696	52.337, 17.310		14896.396, 9492.293	14.430, 12.327	
	SD, SE	8703.3783, 2051.4059	117.9957, 21.5430		12108.0103, 2140.4140	9.3280, 1.5767	
	MEDIAN	14301.685	12.438		11588.641	12.207	
	MIN, MAX	136.475, 30169.969	3.267, 543.506		717.144, 39072.999	3.514, 47.939	
	5%, 95%	136.475, 30169.969	4.007, 388.728		939.306, 37492.941	4.932, 42.076	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	14569.128, 10143.963	89.959, 15.936		15967.596, 10620.017	14.746, 12.694	
	SD, SE	7907.3364, 1863.7771	389.3096, 71.0779		13077.4325, 2348.7762	8.7832, 1.4846	
	MEDIAN	13302.603	10.357		12833.588	13.316	
	MIN, MAX	66.027, 28411.649	3.853, 2148.842		928.893, 58890.910	4.069, 43.944	
	5%, 95%	66.027, 28411.649	5.024, 92.019		1188.489, 36916.112	4.624, 37.976	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	17482.938, 9116.139	21.194, 15.216		16520.707, 12719.280	13.478, 12.521	
	SD, SE	15968.9487, 3873.0390	23.2470, 4.2443		9709.7562, 1803.0565	5.2886, 0.8939	
	MEDIAN	11413.080	13.101		14782.745	12.638	
	MIN, MAX	62.026, 47682.083	4.624, 121.820		587.105, 35443.633	5.795, 29.222	
	5%, 95%	62.026, 47682.083	4.624, 51.848		2589.300, 33956.968	6.103, 24.339	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	15538.848, 10412.604	54.496, 18.515		15318.412, 10829.080	14.218, 12.873	
	SD, SE	9466.5815, 2231.2947	155.5111, 28.3923		10781.3264, 1905.8873	6.4895, 1.0969	
	MEDIAN	14828.367	12.042		11925.487	13.255	
	MIN, MAX	88.176, 32885.249	6.021, 851.919		1001.806, 42595.964	5.960, 29.152	
	5%, 95%	88.176, 32885.249	6.514, 203.248		1063.898, 32642.594	6.042, 29.125	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 105 of 264)

Biomarker: Total Nicotine ((µg/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	177.936, 127.206			148.100, 116.589		
	SD, SE	145.8632, 34.3803			105.9746, 18.7338		
	MEDIAN	145.363			125.143		
	MIN, MAX	7.379, 621.350			23.919, 425.737		
	5%, 95%	7.379, 621.350			36.547, 416.448		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	240.351, 130.331			185.397, 140.480		
	SD, SE	416.7763, 98.2351			153.8084, 27.6248		
	MEDIAN	143.851			121.153		
	MIN, MAX	3.570, 1882.398			38.556, 665.335		
	5%, 95%	3.570, 1882.398			46.464, 569.535		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	192.733, 139.084			181.786, 149.257		
	SD, SE	109.6650, 26.5977			117.1479, 21.7538		
	MEDIAN	193.358			147.533		
	MIN, MAX	3.354, 430.271			23.808, 543.137		
	5%, 95%	3.354, 430.271			54.794, 411.403		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	202.894, 142.171			167.838, 141.197		
	SD, SE	195.6765, 46.1214			105.6447, 18.6755		
	MEDIAN	151.135			136.221		
	MIN, MAX	4.768, 921.368			44.672, 455.706		
	5%, 95%	4.768, 921.368			61.653, 367.479		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 106 of 264)

Biomarker: Total Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1096.978, 784.223			913.037, 718.773		
	SD, SE	899.2469, 211.9545			653.3328, 115.4940		
	MEDIAN	896.160			771.508		
	MIN, MAX	45.492, 3830.625			147.462, 2624.666		
	5%, 95%	45.492, 3830.625			225.314, 2567.399		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1481.766, 803.489			1142.970, 866.060		
	SD, SE	2569.4250, 605.6193			948.2285, 170.3069		
	MEDIAN	886.840			746.906		
	MIN, MAX	22.009, 11604.981			237.698, 4101.790		
	5%, 95%	22.009, 11604.981			286.451, 3511.183		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1188.199, 857.444			1120.711, 920.166		
	SD, SE	676.0857, 163.9749			722.2170, 134.1123		
	MEDIAN	1192.052			909.538		
	MIN, MAX	20.675, 2652.624			146.776, 3348.442		
	5%, 95%	20.675, 2652.624			337.807, 2536.296		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	18		NA	32		NA
	MEAN, GEO MEAN	1250.839, 876.478			1034.721, 870.479		
	SD, SE	1206.3454, 284.3383			651.2997, 115.1346		
	MEDIAN	931.747			839.799		
	MIN, MAX	29.392, 5680.232			275.400, 2809.425		
	5%, 95%	29.392, 5680.232			380.087, 2265.509		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (µg/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.996, 1.221	0.005, NA		2.034, 1.343	0.002, NA	
	SD, SE	2.0759, 0.4893	0.0109, 0.0020		1.5540, 0.2747	0.0018, 0.0003	
	MEDIAN	1.526	0.001		1.792	0.002	
	MIN, MAX	0.021, 9.353	0.000, 0.044		0.097, 5.798	0.000, 0.011	
	5%, 95%	0.021, 9.353	0.000, 0.042		0.100, 5.254	0.001, 0.005	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1.880, 1.210	0.013, NA		2.029, 1.368	0.002, NA	
	SD, SE	1.6531, 0.3896	0.0605, 0.0110		1.7171, 0.3084	0.0014, 0.0002	
	MEDIAN	1.681	0.001		1.752	0.002	
	MIN, MAX	0.012, 7.451	0.000, 0.333		0.130, 7.495	0.000, 0.007	
	5%, 95%	0.012, 7.451	0.000, 0.017		0.144, 6.431	0.001, 0.004	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1.814, 1.068	0.002, NA		2.267, 1.760	0.002, 0.002	
	SD, SE	1.3903, 0.3372	0.0021, 0.0004		1.3884, 0.2578	0.0011, 0.0002	
	MEDIAN	1.555	0.001		2.175	0.002	
	MIN, MAX	0.009, 4.966	0.000, 0.011		0.095, 5.794	0.001, 0.005	
	5%, 95%	0.009, 4.966	0.000, 0.005		0.494, 5.392	0.001, 0.004	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1.899, 1.237	0.007, NA		2.099, 1.497	0.002, NA	
	SD, SE	1.4598, 0.3441	0.0228, 0.0042		1.4870, 0.2629	0.0012, 0.0002	
	MEDIAN	1.741	0.001		1.849	0.002	
	MIN, MAX	0.014, 6.341	0.000, 0.126		0.122, 5.778	0.000, 0.006	
	5%, 95%	0.014, 6.341	0.000, 0.015		0.156, 5.620	0.001, 0.004	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 108 of 264)

Biomarker: Total Nicotine (nmol/mg Creatinine) Analytical Lab: Harrogate							
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	12.307, 7.529	0.031, NA		12.540, 8.279	0.013, NA	
	SD, SE	12.7977, 3.0165	0.0670, 0.0122		9.5803, 1.6936	0.0110, 0.0019	
	MEDIAN	9.408	0.006		11.045	0.012	
	MIN, MAX	0.129, 57.661	0.000, 0.271		0.598, 35.745	0.000, 0.068	
	5%, 95%	0.129, 57.661	0.000, 0.259		0.617, 32.391	0.006, 0.031	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	11.587, 7.457	0.081, NA		12.509, 8.432	0.012, NA	
	SD, SE	10.1915, 2.4022	0.3729, 0.0681		10.5861, 1.9013	0.0086, 0.0014	
	MEDIAN	10.361	0.006		10.801	0.012	
	MIN, MAX	0.074, 45.935	0.000, 2.053		0.801, 46.207	0.000, 0.043	
	5%, 95%	0.074, 45.935	0.000, 0.105		0.888, 39.647	0.006, 0.025	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	11.184, 6.582	0.011, NA		13.978, 10.849	0.012, 0.011	
	SD, SE	8.5709, 2.0788	0.0130, 0.0024		8.5594, 1.5894	0.0067, 0.0011	
	MEDIAN	9.587	0.006		13.409	0.012	
	MIN, MAX	0.055, 30.615	0.000, 0.068		0.586, 35.720	0.006, 0.031	
	5%, 95%	0.055, 30.615	0.000, 0.031		3.046, 33.242	0.006, 0.025	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	11.710, 7.628	0.041, 0.011		12.938, 9.229	0.012, 0.011	
	SD, SE	8.9997, 2.1212	0.1408, 0.0257		9.1678, 1.6207	0.0072, 0.0012	
	MEDIAN	10.731	0.008		11.396	0.010	
	MIN, MAX	0.086, 39.094	0.002, 0.779		0.753, 35.623	0.002, 0.037	
	5%, 95%	0.086, 39.094	0.002, 0.094		0.960, 34.649	0.006, 0.025	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 109 of 264)

Biomarker: Total Nicotine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.211, 0.096			0.122, 0.102		
	SD, SE	0.4228, 0.0997			0.0732, 0.0129		
	MEDIAN	0.092			0.104		
	MIN, MAX	0.007, 1.871			0.028, 0.288		
	5%, 95%	0.007, 1.871			0.033, 0.258		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.302, 0.096			0.144, 0.111		
	SD, SE	0.8571, 0.2020			0.1077, 0.0193		
	MEDIAN	0.089			0.112		
	MIN, MAX	0.004, 3.726			0.029, 0.461		
	5%, 95%	0.004, 3.726			0.033, 0.375		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.139, 0.101			0.155, 0.127		
	SD, SE	0.0991, 0.0240			0.1042, 0.0193		
	MEDIAN	0.113			0.127		
	MIN, MAX	0.003, 0.444			0.024, 0.484		
	5%, 95%	0.003, 0.444			0.047, 0.393		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.216, 0.105			0.141, 0.120		
	SD, SE	0.4526, 0.1067			0.0832, 0.0147		
	MEDIAN	0.103			0.117		
	MIN, MAX	0.005, 2.014			0.031, 0.401		
	5%, 95%	0.005, 2.014			0.044, 0.296		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439277

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 110 of 264)

Biomarker: Total Nicotine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	18		NA	32	NA
	MEAN, GEO MEAN	1.300, 0.593			0.753, 0.627	
	SD, SE	2.6062, 0.6143			0.4505, 0.0796	
	MEDIAN	0.568			0.639	
	MIN, MAX	0.043, 11.532			0.175, 1.776	
	5%, 95%	0.043, 11.532			0.206, 1.592	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	18		NA	31	NA
	MEAN, GEO MEAN	1.860, 0.591			0.887, 0.688	
	SD, SE	5.2830, 1.2452			0.6642, 0.1193	
	MEDIAN	0.549			0.693	
	MIN, MAX	0.025, 22.968			0.178, 2.844	
	5%, 95%	0.025, 22.968			0.205, 2.310	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	17		NA	29	NA
	MEAN, GEO MEAN	0.858, 0.618			0.957, 0.785	
	SD, SE	0.6107, 0.1481			0.6423, 0.1193	
	MEDIAN	0.694			0.781	
	MIN, MAX	0.018, 2.737			0.147, 2.983	
	5%, 95%	0.018, 2.737			0.287, 2.422	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	18		NA	32	NA
	MEAN, GEO MEAN	1.334, 0.646			0.867, 0.741	
	SD, SE	2.7891, 0.6574			0.5133, 0.0907	
	MEDIAN	0.634			0.718	
	MIN, MAX	0.029, 12.412			0.192, 2.473	
	5%, 95%	0.029, 12.412			0.275, 1.824	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 111 of 264)

Biomarker: Total Nicotine (ng/mL) Analytical Lab: Harrogate							
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1588.4, 986.2	3.8, 1.9		1626.2, 879.4	1.2, 1.1	
	SD, SE	1414.79, 333.47	6.34, 1.16		1794.81, 317.28	0.77, 0.13	
	MEDIAN	1284.7	1.0		850.1	1.0	
	MIN, MAX	15.7, 5625.0	1.0, 23.2		42.3, 8096.4	1.0, 5.4	
	5%, 95%	15.7, 5625.0	1.0, 22.6		88.4, 5070.3	1.0, 2.1	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	1772.2, 1162.4	5.9, 1.7		1807.8, 1057.5	1.2, 1.1	
	SD, SE	1309.83, 308.73	22.05, 4.03		2129.81, 382.53	0.57, 0.10	
	MEDIAN	1350.6	1.0		1096.3	1.0	
	MIN, MAX	11.9, 5120.6	1.0, 122.3		103.2, 10733.1	1.0, 3.6	
	5%, 95%	11.9, 5120.6	1.0, 6.8		151.2, 6116.5	1.0, 2.8	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	1439.8, 874.6	1.9, 1.4		1711.5, 1202.2	1.1, 1.0	
	SD, SE	1095.85, 265.78	2.69, 0.49		1316.61, 244.49	0.20, 0.03	
	MEDIAN	939.3	1.0		1317.5	1.0	
	MIN, MAX	9.6, 3515.6	1.0, 15.2		51.2, 4831.6	1.0, 2.1	
	5%, 95%	9.6, 3515.6	1.0, 5.9		300.0, 4652.5	1.0, 1.4	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	1619.5, 1090.0	3.9, 1.9		1662.2, 1039.5	1.1, 1.1	
	SD, SE	1100.15, 259.31	8.86, 1.62		1630.41, 288.22	0.41, 0.07	
	MEDIAN	1178.2	1.1		1264.1	1.0	
	MIN, MAX	12.4, 3783.9	1.0, 48.6		81.6, 7887.0	1.0, 3.0	
	5%, 95%	12.4, 3783.9	1.0, 13.0		163.9, 4037.2	1.0, 2.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 112 of 264)

Biomarker: Total Nicotine (nmol/L) Analytical Lab: Harrogate

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9792.4, 6080.2	23.7, 11.8		10025.6, 5421.7	7.5, 6.9	
	SD, SE	8722.19, 2055.84	39.08, 7.14		11064.98, 1956.03	4.76, 0.81	
	MEDIAN	7919.9	6.2		5240.6	6.2	
	MIN, MAX	96.8, 34678.1	6.2, 143.0		260.8, 49914.3	6.2, 33.3	
	5%, 95%	96.8, 34678.1	6.2, 139.3		545.0, 31258.4	6.2, 12.9	
	# of BLQ/ALQ Values	0/0	15/0		0/0	28/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	10925.7, 7166.2	36.1, 10.3		11145.3, 6519.6	7.3, 6.8	
	SD, SE	8075.10, 1903.32	135.96, 24.82		13130.29, 2358.27	3.54, 0.60	
	MEDIAN	8326.5	6.2		6758.7	6.2	
	MIN, MAX	73.4, 31568.5	6.2, 754.0		636.2, 66169.6	6.2, 22.2	
	5%, 95%	73.4, 31568.5	6.2, 41.9		932.1, 37708.2	6.2, 17.3	
	# of BLQ/ALQ Values	0/0	19/0		0/0	31/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	8876.6, 5391.8	11.8, 8.7		10551.6, 7411.7	6.5, 6.4	
	SD, SE	6755.88, 1638.54	16.59, 3.03		8116.90, 1507.27	1.22, 0.21	
	MEDIAN	5790.8	6.2		8122.4	6.2	
	MIN, MAX	59.2, 21673.7	6.2, 93.7		315.6, 29786.8	6.2, 12.9	
	5%, 95%	59.2, 21673.7	6.2, 36.4		1849.5, 28682.7	6.2, 8.6	
	# of BLQ/ALQ Values	0/0	19/0		0/0	32/0	
Overall*	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	9984.2, 6720.3	23.9, 11.4		10247.7, 6408.1	7.1, 6.8	
	SD, SE	6782.43, 1598.63	54.66, 9.98		10051.53, 1776.88	2.48, 0.42	
	MEDIAN	7263.5	6.7		7793.0	6.2	
	MIN, MAX	76.5, 23327.7	6.2, 299.8		502.8, 48623.6	6.2, 18.3	
	5%, 95%	76.5, 23327.7	6.2, 79.9		1010.2, 24889.6	6.2, 12.5	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 113 of 264)

Biomarker: Total Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	119.3, 77.7			95.4, 66.6		
	SD, SE	116.33, 27.42			84.70, 14.97		
	MEDIAN	90.0			52.5		
	MIN, MAX	5.2, 468.8			18.8, 368.0		
	5%, 95%	5.2, 468.8			19.4, 258.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	177.5, 92.1			120.5, 86.2		
	SD, SE	275.88, 65.03			116.80, 20.98		
	MEDIAN	85.2			77.8		
	MIN, MAX	4.0, 1214.5			24.4, 536.7		
	5%, 95%	4.0, 1214.5			27.8, 403.2		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	120.6, 82.3			119.3, 87.0		
	SD, SE	109.06, 26.45			96.07, 17.84		
	MEDIAN	86.0			89.5		
	MIN, MAX	3.2, 464.9			12.8, 406.8		
	5%, 95%	3.2, 464.9			22.4, 322.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	139.1, 90.8			109.0, 83.2		
	SD, SE	151.24, 35.65			88.36, 15.62		
	MEDIAN	93.2			77.2		
	MIN, MAX	4.1, 667.7			21.9, 408.9		
	5%, 95%	4.1, 667.7			28.7, 282.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 114 of 264)

Biomarker: Total Nicotine ((nmol/L)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	735.4, 479.2			588.2, 410.6		
	SD, SE	717.14, 169.03			522.22, 92.32		
	MEDIAN	554.7			323.3		
	MIN, MAX	32.3, 2889.8			115.8, 2268.8		
	5%, 95%	32.3, 2889.8			119.9, 1593.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1094.0, 567.7			742.9, 531.7		
	SD, SE	1700.73, 400.87			719.99, 129.31		
	MEDIAN	525.1			479.8		
	MIN, MAX	24.5, 7487.1			150.5, 3308.5		
	5%, 95%	24.5, 7487.1			171.5, 2485.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	743.6, 507.1			735.5, 536.2		
	SD, SE	672.35, 163.07			592.33, 109.99		
	MEDIAN	529.9			551.5		
	MIN, MAX	19.7, 2866.2			78.9, 2508.2		
	5%, 95%	19.7, 2866.2			137.9, 1985.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^a	N	18		NA	32		NA
	MEAN, GEO MEAN	857.2, 560.1			671.7, 513.0		
	SD, SE	932.33, 219.75			544.80, 96.31		
	MEDIAN	574.2			475.5		
	MIN, MAX	25.5, 4116.1			134.7, 2521.0		
	5%, 95%	25.5, 4116.1			176.9, 1738.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 115 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5856.477, 3547.473	10.326, 4.671		5682.968, 4198.040	4.083, 2.851	
	SD, SE	4830.8734, 1138.6478	15.7543, 2.8763		4115.0914, 727.4523	4.7968, 0.8108	
	MEDIAN	5526.840	3.426		5379.732	2.725	
	MIN, MAX	42.441, 20367.215	0.950, 67.936		143.550, 18150.580	0.855, 25.488	
	5%, 95%	42.441, 20367.215	1.030, 46.035		935.760, 15778.245	0.880, 13.974	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	5893.470, 3777.184	14.811, 5.527		7035.350, 5370.166	4.484, 3.254	
	SD, SE	3983.1023, 938.8262	29.3232, 5.3537		4427.2664, 795.1605	4.3424, 0.7340	
	MEDIAN	5281.345	3.474		6880.830	2.740	
	MIN, MAX	24.210, 16978.770	0.875, 152.550		400.405, 18154.368	0.750, 20.909	
	5%, 95%	24.210, 16978.770	0.902, 60.135		884.631, 15032.830	1.240, 13.650	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	6143.545, 3478.247	9.735, 4.823		6186.922, 4948.812	3.750, 2.869	
	SD, SE	4990.3866, 1210.3465	15.6351, 2.8546		3791.4769, 704.0596	3.3990, 0.5745	
	MEDIAN	4755.716	2.971		5478.480	2.726	
	MIN, MAX	21.379, 15121.480	1.430, 72.800		976.686, 13569.448	0.990, 16.830	
	5%, 95%	21.379, 15121.480	1.720, 38.750		1154.784, 13029.434	1.068, 10.528	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^a	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	5997.375, 3797.211	11.624, 5.555		6148.123, 4856.528	4.106, 3.207	
	SD, SE	4284.2019, 1009.7961	17.7183, 3.2349		3849.6451, 680.5275	3.3261, 0.5622	
	MEDIAN	5057.474	4.401		5453.019	2.833	
	MIN, MAX	29.343, 17222.174	1.277, 76.940		506.880, 16339.432	1.038, 14.818	
	5%, 95%	29.343, 17222.174	1.374, 56.114		991.725, 12433.240	1.276, 13.701	

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine (nmol/24hr) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	30471.251, 18457.503	53.724, 24.303		29568.484, 21842.404	21.245, 14.836	
	SD, SE	25135.0345, 5924.3844	81.9694, 14.9655		21410.8204, 3784.9341	24.9575, 4.2186	
	MEDIAN	28756.149	17.826		27990.743	14.178	
	MIN, MAX	220.821, 105970.620	4.943, 353.471		746.891, 94437.468	4.449, 132.614	
	5%, 95%	220.821, 105970.620	5.359, 239.520		4868.759, 82094.209	4.579, 72.707	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	30663.727, 19652.694	77.063, 28.756		36604.924, 27940.975	23.328, 16.930	
	SD, SE	20724.0812, 4884.7128	152.5686, 27.8551		23035.0670, 4137.2202	22.5937, 3.8190	
	MEDIAN	27478.838	18.075		35800.958	14.256	
	MIN, MAX	125.965, 88340.540	4.553, 793.718		2083.307, 94457.177	3.902, 108.790	
	5%, 95%	125.965, 88340.540	4.693, 312.882		4602.735, 78215.814	6.452, 71.021	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	31964.866, 18097.321	50.652, 25.096		32190.555, 25748.670	19.510, 14.927	
	SD, SE	25964.9813, 6297.4330	81.3493, 14.8523		19727.0541, 3663.2220	17.6850, 2.9893	
	MEDIAN	24743.990	15.459		28504.531	14.183	
	MIN, MAX	111.235, 78677.060	7.440, 378.778		5081.697, 70601.838	5.151, 87.566	
	5%, 95%	111.235, 78677.060	8.949, 201.616		6008.341, 67792.145	5.557, 54.777	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	31204.341, 19756.903	60.480, 28.902		31988.685, 25268.516	21.361, 16.685	
	SD, SE	22290.7028, 5253.9690	92.1883, 16.8312		20029.7032, 3540.7847	17.3053, 2.9251	
	MEDIAN	26314.038	22.896		28372.055	14.742	
	MIN, MAX	152.674, 89606.973	6.643, 400.319		2637.298, 85014.065	5.402, 77.098	
	5%, 95%	152.674, 89606.973	7.151, 291.961		5159.945, 64690.148	6.639, 71.284	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 117 of 264)

Biomarker: Trans-3-hydroxycotinine ((µg/24hr)/cigarette per day)		Analytical Lab: Harrogate				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	18		NA	32	NA
	MEAN, GEO MEAN	366.392, 279.551			395.623, 317.883	
	SD, SE	186.9103, 44.0552			304.7334, 53.8698	
	MEDIAN	354.907			304.496	
	MIN, MAX	14.147, 678.907			71.775, 1577.825	
	5%, 95%	14.147, 678.907			111.888, 907.529	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	18		NA	31	NA
	MEAN, GEO MEAN	475.134, 299.185			524.203, 437.936	
	SD, SE	539.3469, 127.1253			339.0575, 60.8965	
	MEDIAN	393.913			406.624	
	MIN, MAX	8.070, 2529.445			164.300, 1543.373	
	5%, 95%	8.070, 2529.445			171.498, 1157.695	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	17		NA	29	NA
	MEAN, GEO MEAN	495.498, 327.156			402.474, 358.018	
	SD, SE	337.6115, 81.8828			222.6679, 41.3484	
	MEDIAN	418.213			342.405	
	MIN, MAX	7.126, 1230.107			159.486, 1130.787	
	5%, 95%	7.126, 1230.107			168.022, 868.629	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	18		NA	32	NA
	MEAN, GEO MEAN	443.352, 314.371			442.515, 381.049	
	SD, SE	301.6047, 71.0889			267.3219, 47.2563	
	MEDIAN	426.221			371.095	
	MIN, MAX	9.781, 1385.359			148.070, 1322.233	
	5%, 95%	9.781, 1385.359			152.052, 1006.597	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 118 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1906.337, 1454.505			2058.426, 1653.945		
	SD, SE	972.4943, 229.2191			1585.5276, 280.2843		
	MEDIAN	1846.580			1584.293		
	MIN, MAX	73.607, 3532.354			373.446, 8209.421		
	5%, 95%	73.607, 3532.354			582.154, 4721.873		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2472.124, 1556.661			2727.427, 2278.579		
	SD, SE	2806.2222, 661.4329			1764.1162, 316.8446		
	MEDIAN	2049.526			2115.666		
	MIN, MAX	41.988, 13160.703			854.853, 8030.171		
	5%, 95%	41.988, 13160.703			892.302, 6023.487		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2578.077, 1702.195			2094.073, 1862.767		
	SD, SE	1756.5924, 426.0362			1158.5411, 215.1357		
	MEDIAN	2175.964			1781.533		
	MIN, MAX	37.078, 6400.244			829.805, 5883.487		
	5%, 95%	37.078, 6400.244			874.221, 4519.476		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2306.758, 1635.674			2302.404, 1982.596		
	SD, SE	1569.2492, 369.8756			1390.8757, 245.8744		
	MEDIAN	2217.627			1930.806		
	MIN, MAX	50.891, 7208.023			770.409, 6879.578		
	5%, 95%	50.891, 7208.023			791.127, 5237.322		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 119 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4.056, 2.684	0.006, NA		5.165, 3.661	0.004, 0.003	
	SD, SE	2.5920, 0.6109	0.0097, 0.0018		3.8502, 0.6806	0.0062, 0.0011	
	MEDIAN	4.045	0.002		4.391	0.002	
	MIN, MAX	0.040, 8.886	0.000, 0.042		0.119, 14.351	0.001, 0.036	
	5%, 95%	0.040, 8.886	0.001, 0.032		0.500, 13.466	0.001, 0.016	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	4.195, 2.776	0.009, NA		5.733, 4.264	0.004, 0.003	
	SD, SE	2.6525, 0.6252	0.0172, 0.0031		4.0709, 0.7312	0.0042, 0.0007	
	MEDIAN	3.834	0.003		4.761	0.002	
	MIN, MAX	0.027, 10.012	0.000, 0.079		0.400, 15.297	0.001, 0.019	
	5%, 95%	0.027, 10.012	0.001, 0.057		0.693, 14.865	0.001, 0.018	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	4.141, 2.512	0.005, 0.003		5.557, 4.221	0.004, 0.002	
	SD, SE	2.9060, 0.7048	0.0082, 0.0015		4.0050, 0.7437	0.0039, 0.0007	
	MEDIAN	3.299	0.002		4.139	0.002	
	MIN, MAX	0.019, 9.708	0.001, 0.041		0.770, 15.542	0.001, 0.022	
	5%, 95%	0.019, 9.708	0.001, 0.018		0.972, 11.857	0.001, 0.008	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	4.143, 2.740	0.007, 0.003		5.436, 4.136	0.004, 0.003	
	SD, SE	2.6080, 0.6147	0.0100, 0.0018		3.8060, 0.6728	0.0040, 0.0007	
	MEDIAN	3.555	0.003		4.286	0.002	
	MIN, MAX	0.029, 9.245	0.001, 0.037		0.497, 14.264	0.001, 0.019	
	5%, 95%	0.029, 9.245	0.001, 0.033		0.654, 12.984	0.001, 0.017	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 120 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine) Analytical Lab: Harrogate

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	21.104, 13.962	0.032, NA		26.874, 19.047	0.020, 0.013	
	SD, SE	13.4863, 3.1788	0.0505, 0.0092		20.0325, 3.5413	0.0325, 0.0055	
	MEDIAN	21.044	0.010		22.847	0.010	
	MIN, MAX	0.208, 46.234	0.000, 0.219		0.619, 74.668	0.005, 0.187	
	5%, 95%	0.208, 46.234	0.005, 0.166		2.602, 70.064	0.005, 0.083	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	21.828, 14.439	0.047, NA		29.830, 22.188	0.020, 0.014	
	SD, SE	13.8009, 3.2529	0.0898, 0.0164		21.1808, 3.8042	0.0220, 0.0037	
	MEDIAN	19.946	0.013		24.771	0.010	
	MIN, MAX	0.140, 52.092	0.000, 0.411		2.081, 79.590	0.005, 0.099	
	5%, 95%	0.140, 52.092	0.005, 0.297		3.606, 77.343	0.005, 0.094	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	21.545, 13.070	0.026, 0.013		28.915, 21.960	0.018, 0.013	
	SD, SE	15.1200, 3.6671	0.0427, 0.0078		20.8379, 3.8695	0.0201, 0.0034	
	MEDIAN	17.165	0.010		21.535	0.010	
	MIN, MAX	0.099, 50.511	0.005, 0.213		4.006, 80.865	0.005, 0.114	
	5%, 95%	0.099, 50.511	0.005, 0.094		5.057, 61.692	0.005, 0.042	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	21.558, 14.243	0.035, 0.016		28.284, 21.519	0.019, 0.014	
	SD, SE	13.5702, 3.1985	0.0521, 0.0095		19.8026, 3.5006	0.0206, 0.0035	
	MEDIAN	18.494	0.013		22.298	0.012	
	MIN, MAX	0.149, 48.103	0.003, 0.194		2.586, 74.215	0.005, 0.099	
	5%, 95%	0.149, 48.103	0.003, 0.170		3.405, 67.557	0.005, 0.088	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall!
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Biomarker: Trans-3-hydroxycotinine (($\mu\text{g}/\text{mg}$ Creatinine)/cigarette per day) Analytical Lab: Harrogate

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	0.324, 0.211			0.350, 0.277		
	SD, SE	0.3761, 0.0887			0.2673, 0.0472		
	MEDIAN	0.245			0.290		
	MIN, MAX	0.013, 1.777			0.060, 1.347		
	5%, 95%	0.013, 1.777			0.109, 0.957		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.498, 0.220			0.422, 0.348		
	SD, SE	1.1285, 0.2660			0.2621, 0.0471		
	MEDIAN	0.262			0.364		
	MIN, MAX	0.009, 5.006			0.094, 1.070		
	5%, 95%	0.009, 5.006			0.130, 0.914		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	0.385, 0.236			0.370, 0.305		
	SD, SE	0.3970, 0.0963			0.2805, 0.0521		
	MEDIAN	0.286			0.265		
	MIN, MAX	0.006, 1.768			0.107, 1.482		
	5%, 95%	0.006, 1.768			0.136, 0.928		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.400, 0.227			0.386, 0.324		
	SD, SE	0.6208, 0.1463			0.2494, 0.0441		
	MEDIAN	0.277			0.347		
	MIN, MAX	0.009, 2.850			0.116, 1.170		
	5%, 95%	0.009, 2.850			0.136, 1.063		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 122 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1.683, 1.100			1.819, 1.442		
	SD, SE	1.9572, 0.4613			1.3902, 0.2458		
	MEDIAN	1.275			1.506		
	MIN, MAX	0.069, 9.247			0.310, 7.006		
	5%, 95%	0.069, 9.247			0.567, 4.979		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2.593, 1.144			2.197, 1.810		
	SD, SE	5.8717, 1.3840			1.3636, 0.2449		
	MEDIAN	1.361			1.896		
	MIN, MAX	0.047, 26.046			0.487, 5.568		
	5%, 95%	0.047, 26.046			0.677, 4.754		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2.004, 1.229			1.926, 1.589		
	SD, SE	2.0651, 0.5009			1.4600, 0.2711		
	MEDIAN	1.487			1.377		
	MIN, MAX	0.033, 9.197			0.558, 7.712		
	5%, 95%	0.033, 9.197			0.708, 4.830		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2.079, 1.187			2.009, 1.686		
	SD, SE	3.2305, 0.7614			1.2974, 0.2294		
	MEDIAN	1.438			1.807		
	MIN, MAX	0.050, 14.830			0.603, 6.086		
	5%, 95%	0.050, 14.830			0.707, 5.530		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 123 of 264)

Biomarker: Trans-3-hydroxycotinine (ng/mL)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3751.4, 2167.4	6.9, 3.2		3436.3, 2397.8	2.3, 1.6	
	SD, SE	3939.23, 928.49	13.99, 2.55		2714.78, 479.91	3.19, 0.54	
	MEDIAN	3027.7	3.0		3110.5	1.1	
	MIN, MAX	30.1, 17333.8	1.0, 77.2		52.2, 12964.7	1.0, 17.7	
	5%, 95%	30.1, 17333.8	1.0, 16.5		422.2, 9882.6	1.0, 10.2	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	4429.1, 2668.3	10.6, 3.6		4838.9, 3296.8	2.4, 1.7	
	SD, SE	4222.63, 995.28	25.38, 4.63		3905.64, 701.47	2.85, 0.48	
	MEDIAN	3357.9	2.5		3464.4	1.2	
	MIN, MAX	26.9, 18865.3	1.0, 135.0		219.4, 13348.8	1.0, 15.9	
	5%, 95%	26.9, 18865.3	1.0, 45.6		731.1, 13308.1	1.0, 7.0	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	3384.2, 2057.2	5.5, 2.7		3785.0, 2883.8	1.9, 1.5	
	SD, SE	2434.95, 590.56	10.33, 1.89		3055.44, 567.38	1.87, 0.32	
	MEDIAN	3560.9	2.2		3001.5	1.0	
	MIN, MAX	20.4, 9253.1	1.0, 56.0		525.1, 15599.2	1.0, 9.7	
	5%, 95%	20.4, 9253.1	1.0, 17.1		627.6, 8394.0	1.0, 5.8	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	3908.9, 2541.6	7.7, 3.6		3939.4, 2916.7	2.2, 1.7	
	SD, SE	2969.07, 699.82	13.00, 2.37		2952.97, 522.02	2.04, 0.35	
	MEDIAN	3787.3	2.9		3063.3	1.4	
	MIN, MAX	25.8, 13647.0	1.0, 52.6		265.6, 13970.9	1.0, 9.0	
	5%, 95%	25.8, 13647.0	1.0, 51.5		601.4, 8965.5	1.0, 8.8	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

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Table 14.2.1-2
Statistical Comparison Between Smokers and Non-Smokers of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 122 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg creatinine)/cigarette per day		Analytical Lab: Harrogate		P-value ^a
Timepoint	Statistic	Smokers	Non-Smokers	
Week 1	N	50		NA
	MEAN, GEO MEAN	1,771, 1,308		
	SD, SE	1,5987, 0.2261		
	MEDIAN	1,384		
	MIN, MAX	0.069, 9.247		
	5%, 95%	0.310, 4.979		
	# of BLQ/ALQ Values	0/0		
Week 2	N	49		NA
	MEAN, GEO MEAN	2,342, 1,529		
	SD, SE	3,6619, 0.5231		
	MEDIAN	1,485		
	MIN, MAX	0.047, 26.046		
	5%, 95%	0.487, 4.754		
	# of BLQ/ALQ Values	0/0		
Week 3	N	46		NA
	MEAN, GEO MEAN	1,955, 1,445		
	SD, SE	1,6865, 0.2487		
	MEDIAN	1,452		
	MIN, MAX	0.033, 9.197		
	5%, 95%	0.558, 4.830		
	# of BLQ/ALQ Values	0/0		
Overall ^b	N	50		NA
	MEAN, GEO MEAN	2,034, 1,486		
	SD, SE	2,1649, 0.3062		
	MEDIAN	1,622		
	MIN, MAX	0.050, 14.830		
	5%, 95%	0.603, 5.530		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1,234' will be used as '1,234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((ng/mL)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	236.4, 170.8			237.3, 181.6		
	SD, SE	159.94, 37.70			181.16, 32.03		
	MEDIAN	219.9			184.0		
	MIN, MAX	10.0, 577.8			26.1, 648.2		
	5%, 95%	10.0, 577.8			52.4, 644.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	359.9, 211.4			354.4, 268.9		
	SD, SE	391.10, 92.18			296.14, 53.19		
	MEDIAN	278.2			271.8		
	MIN, MAX	9.0, 1631.9			82.2, 1486.8		
	5%, 95%	9.0, 1631.9			90.2, 935.4		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	354.0, 193.5			254.4, 208.6		
	SD, SE	440.18, 106.76			183.85, 34.14		
	MEDIAN	217.5			191.1		
	MIN, MAX	6.8, 1850.6			65.3, 824.1		
	5%, 95%	6.8, 1850.6			92.3, 678.2		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	315.8, 208.4			286.6, 228.0		
	SD, SE	281.77, 66.41			217.07, 38.37		
	MEDIAN	297.1			221.2		
	MIN, MAX	8.6, 1263.3			78.0, 1012.3		
	5%, 95%	8.6, 1263.3			80.8, 801.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine ((nmol/L)/cigarette per day)			Analytical Lab: Harrogate				
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	1229.8, 888.7			1234.7, 944.7		
	SD, SE	832.19, 196.15			942.62, 166.63		
	MEDIAN	1143.9			957.4		
	MIN, MAX	52.2, 3006.3			135.8, 3372.8		
	5%, 95%	52.2, 3006.3			272.8, 3350.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	1872.6, 1099.7			1843.9, 1398.8		
	SD, SE	2034.94, 479.64			1540.80, 276.74		
	MEDIAN	1447.6			1414.4		
	MIN, MAX	46.7, 8490.8			427.4, 7735.9		
	5%, 95%	46.7, 8490.8			469.1, 4866.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	1841.9, 1006.8			1323.7, 1085.5		
	SD, SE	2290.26, 555.47			956.59, 177.63		
	MEDIAN	1131.4			994.3		
	MIN, MAX	35.4, 9628.8			339.8, 4287.7		
	5%, 95%	35.4, 9628.8			480.3, 3528.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	1642.8, 1084.4			1491.0, 1186.4		
	SD, SE	1466.11, 345.57			1129.38, 199.65		
	MEDIAN	1545.7			1150.8		
	MIN, MAX	44.8, 6573.1			405.8, 5266.8		
	5%, 95%	44.8, 6573.1			420.3, 4168.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 127 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/24hr)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	25	<.0001	31	28	<.0001
	MEAN, GEO MEAN	13658.845, 7347.445	14.677, NA		9608.180, 6681.409	4.439, NA	
	SD, SE	14825.1638, 3494.3246	23.1053, 4.6211		6687.0304, 1201.0261	6.9324, 1.3101	
	MEDIAN	8980.785	5.640		8366.015	1.460	
	MIN, MAX	197.400, 56537.828	0.000, 86.504		218.900, 26230.442	0.000, 30.003	
	5%, 95%	197.400, 56537.828	0.000, 72.540		757.770, 25398.680	0.000, 16.900	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	27	<.0001	31	32	<.0001
	MEAN, GEO MEAN	9769.276, 6028.731	21.598, NA		10395.111, 7947.637	6.978, NA	
	SD, SE	8845.0262, 2084.7927	41.6044, 8.0068		6743.3354, 1211.1388	13.3339, 2.3571	
	MEDIAN	7733.962	3.198		9075.575	1.247	
	MIN, MAX	126.000, 38811.750	0.000, 202.270		540.383, 26263.300	0.000, 62.122	
	5%, 95%	126.000, 38811.750	0.000, 75.525		1494.592, 24231.808	0.000, 31.536	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	28	<.0001	28	33	<.0001
	MEAN, GEO MEAN	12597.302, 6606.374	13.923, NA		12135.876, 9285.056	3.619, NA	
	SD, SE	14947.9926, 3625.4207	25.7235, 4.8613		8852.0829, 1672.8864	6.9289, 1.2062	
	MEDIAN	8891.740	3.172		8279.226	0.000	
	MIN, MAX	160.868, 64170.700	0.000, 88.660		1725.522, 33098.780	0.000, 26.235	
	5%, 95%	160.868, 64170.700	0.000, 86.250		2950.624, 31402.440	0.000, 25.331	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall*	N	18	30	<.0001	32	34	<.0001
	MEAN, GEO MEAN	12023.216, 7040.189	16.131, NA		10289.617, 8058.196	4.676, NA	
	SD, SE	11899.5072, 2804.7407	26.2059, 4.7845		6756.9201, 1194.4660	7.1303, 1.2228	
	MEDIAN	8821.495	4.403		9018.318	1.493	
	MIN, MAX	161.423, 49042.882	0.000, 104.787		828.268, 27010.976	0.000, 28.585	
	5%, 95%	161.423, 49042.882	0.000, 87.582		1717.542, 23927.143	0.000, 23.501	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 128 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	790.341, 579.000			641.220, 504.367		
	SD, SE	482.4312, 113.7101			426.1668, 76.5418		
	MEDIAN	749.353			577.122		
	MIN, MAX	43.617, 1884.594			50.518, 1748.696		
	5%, 95%	43.617, 1884.594			109.450, 1670.809		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	818.142, 477.527			779.872, 648.128		
	SD, SE	1183.1622, 278.8740			510.0117, 91.6008		
	MEDIAN	597.251			658.215		
	MIN, MAX	34.585, 5423.915			175.088, 2470.428		
	5%, 95%	34.585, 5423.915			188.836, 1661.556		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	28		NA
	MEAN, GEO MEAN	992.994, 621.382			728.723, 647.763		
	SD, SE	842.3096, 204.2901			346.7906, 65.5373		
	MEDIAN	671.104			704.582		
	MIN, MAX	35.637, 3329.928			236.928, 1499.048		
	5%, 95%	35.637, 3329.928			283.565, 1439.077		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	860.239, 589.759			718.150, 636.223		
	SD, SE	724.0995, 170.6719			360.2247, 63.6793		
	MEDIAN	795.931			632.731		
	MIN, MAX	37.946, 3355.093			230.597, 1704.335		
	5%, 95%	37.946, 3355.093			265.373, 1545.608		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 129 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	25	<.0001	31	28	<.0001
	MEAN, GEO MEAN	9.316, 5.558	0.009, NA		8.742, 5.873	0.004, NA	
	SD, SE	8.9395, 2.1071	0.0145, 0.0029		6.9972, 1.2567	0.0071, 0.0013	
	MEDIAN	7.365	0.002		6.599	0.001	
	MIN, MAX	0.186, 37.904	0.000, 0.053		0.182, 24.795	0.000, 0.034	
	5%, 95%	0.186, 37.904	0.000, 0.051		0.724, 24.215	0.000, 0.015	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	27	<.0001	31	32	<.0001
	MEAN, GEO MEAN	7.764, 4.431	0.013, NA		8.681, 6.311	0.006, NA	
	SD, SE	8.8779, 2.0925	0.0244, 0.0047		7.1363, 1.2817	0.0118, 0.0021	
	MEDIAN	4.949	0.002		6.791	0.001	
	MIN, MAX	0.141, 37.773	0.000, 0.105		0.539, 31.266	0.000, 0.053	
	5%, 95%	0.141, 37.773	0.000, 0.072		1.171, 24.592	0.000, 0.041	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	28	<.0001	28	33	<.0001
	MEAN, GEO MEAN	9.048, 4.767	0.007, NA		10.684, 7.829	0.003, NA	
	SD, SE	10.5051, 2.5479	0.0127, 0.0024		9.3656, 1.7699	0.0071, 0.0012	
	MEDIAN	6.526	0.002		7.318	0.000	
	MIN, MAX	0.141, 41.198	0.000, 0.050		1.718, 40.332	0.000, 0.034	
	5%, 95%	0.141, 41.198	0.000, 0.040		1.968, 30.778	0.000, 0.018	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	34	<.0001
	MEAN, GEO MEAN	8.691, 5.073	0.009, NA		9.174, 6.798	0.004, NA	
	SD, SE	9.1846, 2.1648	0.0147, 0.0027		7.2907, 1.2888	0.0072, 0.0012	
	MEDIAN	5.838	0.002		6.767	0.001	
	MIN, MAX	0.156, 38.958	0.000, 0.052		0.813, 30.859	0.000, 0.036	
	5%, 95%	0.156, 38.958	0.000, 0.049		1.351, 26.074	0.000, 0.021	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 130 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine)/cigarette per day		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	0.691, 0.438			0.577, 0.443		
	SD, SE	0.8481, 0.1999			0.4797, 0.0862		
	MEDIAN	0.550			0.466		
	MIN, MAX	0.020, 3.948			0.091, 2.480		
	5%, 95%	0.020, 3.948			0.125, 1.523		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	0.960, 0.351			0.637, 0.515		
	SD, SE	2.4506, 0.5776			0.4155, 0.0746		
	MEDIAN	0.349			0.497		
	MIN, MAX	0.018, 10.734			0.135, 1.832		
	5%, 95%	0.018, 10.734			0.146, 1.381		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	28		NA
	MEAN, GEO MEAN	0.861, 0.449			0.637, 0.546		
	SD, SE	1.2923, 0.3134			0.3551, 0.0671		
	MEDIAN	0.577			0.525		
	MIN, MAX	0.020, 5.679			0.225, 1.344		
	5%, 95%	0.020, 5.679			0.229, 1.231		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	0.828, 0.427			0.627, 0.537		
	SD, SE	1.5066, 0.3551			0.3666, 0.0648		
	MEDIAN	0.531			0.503		
	MIN, MAX	0.019, 6.787			0.177, 1.697		
	5%, 95%	0.019, 6.787			0.247, 1.316		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 131 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/L) Analytical Lab: Harrogate

Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	18	25	<.0001	31	28	<.0001
	MEAN, GEO MEAN	8694.8, 4489.1	9.6, NA		5851.2, 3777.8	2.8, NA	
	SD, SE	11055.18, 2605.73	19.76, 3.95		4628.53, 831.31	4.66, 0.88	
	MEDIAN	5531.3	3.6		4515.7	1.0	
	MIN, MAX	140.0, 48117.3	0.0, 98.3		79.6, 16292.2	0.0, 21.9	
	5%, 95%	140.0, 48117.3	0.0, 26.0		649.9, 14940.4	0.0, 9.9	
	# of BLQ/ALQ Values	0/0	7/0		0/0	15/0	
Week 2	N	18	27	<.0001	31	32	<.0001
	MEAN, GEO MEAN	6920.4, 4258.9	15.0, NA		6590.7, 4879.1	3.6, NA	
	SD, SE	5859.62, 1381.13	35.65, 6.86		4718.06, 847.39	6.99, 1.24	
	MEDIAN	5673.1	1.6		5492.3	0.8	
	MIN, MAX	140.0, 23215.8	0.0, 179.0		296.1, 18931.1	0.0, 34.9	
	5%, 95%	140.0, 23215.8	0.0, 62.4		1061.9, 15749.0	0.0, 15.6	
	# of BLQ/ALQ Values	0/0	3/0		0/0	14/0	
Week 3	N	17	28	<.0001	28	33	<.0001
	MEAN, GEO MEAN	7528.7, 3907.3	7.6, NA		7528.8, 5371.4	1.9, NA	
	SD, SE	8771.50, 2127.40	14.35, 2.71		7767.25, 1467.87	3.49, 0.61	
	MEDIAN	5225.9	2.1		4873.4	0.0	
	MIN, MAX	153.5, 29731.5	0.0, 68.2		927.7, 40612.0	0.0, 14.6	
	5%, 95%	153.5, 29731.5	0.0, 27.6		1603.6, 16665.7	0.0, 9.9	
	# of BLQ/ALQ Values	0/0	8/0		0/0	22/0	
Overall ^b	N	18	30	<.0001	32	34	<.0001
	MEAN, GEO MEAN	7766.0, 4760.1	10.7, NA		6416.1, 4776.7	2.6, NA	
	SD, SE	6698.46, 1578.84	19.45, 3.55		4868.46, 860.63	4.01, 0.69	
	MEDIAN	6527.5	4.0		4925.5	1.1	
	MIN, MAX	144.5, 25999.9	0.0, 83.3		434.5, 22446.3	0.0, 17.4	
	5%, 95%	144.5, 25999.9	0.0, 71.1		855.9, 14963.3	0.0, 13.2	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 132 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/L/cigarette per day)		Analytical Lab: Harrogate					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	31		NA
	MEAN, GEO MEAN	518.8, 353.8			383.7, 285.2		
	SD, SE	424.26, 100.00			291.81, 52.41		
	MEDIAN	412.5			341.5		
	MIN, MAX	46.7, 1603.9			39.8, 1128.9		
	5%, 95%	46.7, 1603.9			58.1, 1086.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	611.5, 337.3			495.5, 397.9		
	SD, SE	815.54, 192.22			391.89, 70.39		
	MEDIAN	378.9			389.8		
	MIN, MAX	33.1, 3499.3			153.1, 2142.1		
	5%, 95%	33.1, 3499.3			160.9, 1018.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	28		NA
	MEAN, GEO MEAN	815.2, 367.5			462.5, 374.7		
	SD, SE	1394.96, 338.33			342.98, 64.82		
	MEDIAN	382.3			361.7		
	MIN, MAX	15.5, 5946.3			125.4, 1765.7		
	5%, 95%	15.5, 5946.3			153.2, 848.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	642.4, 394.8			451.5, 376.2		
	SD, SE	745.77, 175.78			285.16, 50.41		
	MEDIAN	491.9			356.1		
	MIN, MAX	35.6, 3376.2			139.4, 1256.7		
	5%, 95%	35.6, 3376.2			156.4, 1034.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 133 of 264)

Biomarker: Cotinine (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	7447.932, 6580.248	12,002, 9,306		8784.549, 8271.044	6,909, 6,393	
	SD, SE	3854.3433, 2225.3061	10,708.1, 5,354.0		3413.1486, 1970.5823	3,115.3, 1,798.6	
	MEDIAN	8796.396	7,812		9681.650	7,062	
	MIN, MAX	3100.528, 10446.873	4,588, 27,797		5012.448, 11659.550	3,720, 9,945	
	5%, 95%	3100.528, 10446.873	4,588, 27,797		5012.448, 11659.550	3,720, 9,945	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0497	3	4	0.0318
	MEAN, GEO MEAN	6966.875, 6705.083	6,983, 6,752		10347.571, 9953.407	7,374, 6,742	
	SD, SE	2243.0815, 1295.0437	2,058.1, 1,029.0		3472.8274, 2005.0379	3,158.1, 1,579.1	
	MEDIAN	7302.803	6,867		10101.990	7,867	
	MIN, MAX	4574.775, 9023.046	5,208, 8,990		7004.052, 13936.670	3,224, 10,540	
	5%, 95%	4574.775, 9023.046	5,208, 8,990		7004.052, 13936.670	3,224, 10,540	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1489	3	4	0.0518
	MEAN, GEO MEAN	7079.085, 5030.830	6,989, 6,847		7500.506, 7079.276	6,053, 5,664	
	SD, SE	7043.3216, 4980.3805	1,780.2, 1,027.8		2979.9043, 1720.4485	2,698.9, 1,349.4	
	MEDIAN	7079.085	6,398		7564.865	5,193	
	MIN, MAX	2098.704, 12059.465	5,580, 8,990		4488.944, 10447.710	3,906, 9,920	
	5%, 95%	2098.704, 12059.465	5,580, 8,990		4488.944, 10447.710	3,906, 9,920	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	7272.466, 6507.886	8,819, 8,419		8877.542, 8499.398	6,885, 6,463	
	SD, SE	3687.8285, 2129.1688	3,162.9, 1,581.4		2928.4631, 1690.7489	2,597.9, 1,298.9	
	MEDIAN	8049.600	8,218		10394.395	7,165	
	MIN, MAX	3258.002, 10509.795	5,704, 13,134		5501.815, 10736.417	3,617, 9,593	
	5%, 95%	3258.002, 10509.795	5,704, 13,134		5501.815, 10736.417	3,617, 9,593	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 134 of 264)

Biomarker: Cotinine (µg/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	1312.326, 1159.440	2.115, 1.640		1547.838, 1457.358	1.217, 1.126	
	SD, SE	679.1353, 392.0989	1.8870, 0.9435		601.3971, 347.2168	0.5490, 0.3170	
	MEDIAN	1549.925	1.377		1705.907	1.244	
	MIN, MAX	546.313, 1840.739	0.808, 4.898		883.193, 2054.413	0.655, 1.752	
	5%, 95%	546.313, 1840.739	0.808, 4.898		883.193, 2054.413	0.655, 1.752	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0497	3	4	0.0518
	MEAN, GEO MEAN	1227.563, 1181.436	1.231, 1.190		1823.242, 1753.790	1.299, 1.188	
	SD, SE	395.2313, 228.1869	0.3624, 0.1812		611.9120, 353.2876	0.5563, 0.2782	
	MEDIAN	1286.754	1.210		1779.971	1.386	
	MIN, MAX	806.075, 1589.861	0.918, 1.584		1234.114, 2455.641	0.568, 1.857	
	5%, 95%	806.075, 1589.861	0.918, 1.584		1234.114, 2455.641	0.568, 1.857	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1489	3	4	0.0518
	MEAN, GEO MEAN	1247.335, 886.433	1.231, 1.206		1321.589, 1247.368	1.067, 0.998	
	SD, SE	1241.0332, 877.5430	0.3138, 0.1812		525.0593, 303.1432	0.4756, 0.2378	
	MEDIAN	1247.335	1.127		1332.929	0.915	
	MIN, MAX	369.792, 2124.878	0.983, 1.584		790.952, 1840.887	0.688, 1.748	
	5%, 95%	369.792, 2124.878	0.983, 1.584		790.952, 1840.887	0.688, 1.748	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	1281.409, 1146.690	1.554, 1.483		1564.223, 1497.594	1.213, 1.139	
	SD, SE	649.7955, 375.1596	0.5573, 0.2786		515.9951, 297.9099	0.4578, 0.2289	
	MEDIAN	1418.340	1.448		1831.492	1.263	
	MIN, MAX	574.060, 1851.826	1.005, 2.314		969.420, 1891.757	0.637, 1.690	
	5%, 95%	574.060, 1851.826	1.005, 2.314		969.420, 1891.757	0.637, 1.690	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 135 of 264)

Biomarker: Cotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	589.927, 556.189			371.957, 362.484		
	SD, SE	252.1529, 145.5806			104.0663, 60.0827		
	MEDIAN	516.755			353.320		
	MIN, MAX	382.452, 870.573			278.469, 484.083		
	5%, 95%	382.452, 870.573			278.469, 484.083		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	547.632, 515.541			910.234, 743.421		
	SD, SE	240.5892, 138.9043			691.8706, 399.4517		
	MEDIAN	457.478			696.834		
	MIN, MAX	365.140, 820.277			350.203, 1683.665		
	5%, 95%	365.140, 820.277			350.203, 1683.665		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	677.370, 592.889			789.638, 547.651		
	SD, SE	463.2759, 327.5855			826.6650, 477.2753		
	MEDIAN	677.370			378.243		
	MIN, MAX	349.784, 1004.955			249.386, 1741.285		
	5%, 95%	349.784, 1004.955			249.386, 1741.285		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	571.246, 529.247			690.610, 576.476		
	SD, SE	285.5033, 164.8354			505.5171, 291.8604		
	MEDIAN	441.339			519.720		
	MIN, MAX	373.796, 898.602			292.686, 1259.423		
	5%, 95%	373.796, 898.602			292.686, 1259.423		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 136 of 264)

Biomarker: Cotinine ((µg/24hr)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	103.945, 98.000			65.539, 63.869		
	SD, SE	44.4294, 25.6513			18.3364, 10.5865		
	MEDIAN	91.052			62.255		
	MIN, MAX	67.388, 153.395			49.066, 85.295		
	5%, 95%	67.388, 153.395			49.066, 85.295		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	96.493, 90.839			160.383, 130.991		
	SD, SE	42.3917, 24.4749			121.9077, 70.3834		
	MEDIAN	80.608			122.782		
	MIN, MAX	64.338, 144.533			61.706, 296.662		
	5%, 95%	64.338, 144.533			61.706, 296.662		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	119.353, 104.467			139.134, 96.496		
	SD, SE	81.6291, 57.7205			145.6588, 84.0961		
	MEDIAN	119.353			66.646		
	MIN, MAX	61.632, 177.073			43.942, 306.815		
	5%, 95%	61.632, 177.073			43.942, 306.815		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	100.654, 93.253			121.685, 101.575		
	SD, SE	50.3058, 29.0441			89.0727, 51.4262		
	MEDIAN	77.764			91.574		
	MIN, MAX	65.863, 158.334			51.571, 221.911		
	5%, 95%	65.863, 158.334			51.571, 221.911		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 137 of 264)

Biomarker: Cotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0518	3	3	0.0765
	MEAN, GEO MEAN	4.952, 4.530	0.006, 0.005		7.459, 6.305	0.007, 0.006	
	SD, SE	2.3935, 1.3819	0.0041, 0.0020		4.4571, 2.5733	0.0029, 0.0017	
	MEDIAN	4.962	0.005		8.305	0.005	
	MIN, MAX	2.553, 7.340	0.003, 0.012		2.640, 11.433	0.005, 0.010	
	5%, 95%	2.553, 7.340	0.003, 0.012		2.640, 11.433	0.005, 0.010	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0497	3	4	0.0518
	MEAN, GEO MEAN	5.895, 5.703	0.004, 0.004		8.269, 7.266	0.007, 0.006	
	SD, SE	1.9382, 1.1190	0.0016, 0.0008		5.2339, 3.0218	0.0034, 0.0017	
	MEDIAN	4.778	0.004		6.393	0.006	
	MIN, MAX	4.774, 8.133	0.002, 0.006		4.231, 14.182	0.003, 0.011	
	5%, 95%	4.774, 8.133	0.002, 0.006		4.231, 14.182	0.003, 0.011	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1386	3	4	0.0497
	MEAN, GEO MEAN	6.742, 6.040	0.005, 0.005		6.759, 6.029	0.006, 0.005	
	SD, SE	4.2370, 2.9960	0.0012, 0.0007		3.5104, 2.0267	0.0017, 0.0009	
	MEDIAN	6.742	0.006		7.282	0.006	
	MIN, MAX	3.746, 9.738	0.004, 0.006		3.016, 9.978	0.003, 0.007	
	5%, 95%	3.746, 9.738	0.004, 0.006		3.016, 9.978	0.003, 0.007	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	3	4	0.0497	3	4	0.0518
	MEAN, GEO MEAN	5.655, 5.326	0.005, 0.005		7.496, 6.674	0.007, 0.006	
	SD, SE	2.4525, 1.4160	0.0008, 0.0004		3.8867, 2.2440	0.0024, 0.0012	
	MEDIAN	4.868	0.005		8.225	0.007	
	MIN, MAX	3.692, 8.404	0.004, 0.006		3.296, 10.966	0.004, 0.009	
	5%, 95%	3.692, 8.404	0.004, 0.006		3.296, 10.966	0.004, 0.009	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234^a will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 138 of 264)

Biomarker: Cotinine (µg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0436	3	3	0.0765
	MEAN, GEO MEAN	0.872, 0.798	0.001, 0.001		1.314, 1.111	0.001, 0.001	
	SD, SE	0.4215, 0.2434	0.0005, 0.0003		0.7852, 0.4533	0.0006, 0.0003	
	MEDIAN	0.874	0.001		1.463	0.001	
	MIN, MAX	0.450, 1.293	0.001, 0.002		0.465, 2.014	0.001, 0.002	
	5%, 95%	0.450, 1.293	0.001, 0.002		0.465, 2.014	0.001, 0.002	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0436	3	4	0.0436
	MEAN, GEO MEAN	1.039, 1.005	0.001, NA		1.457, 1.280	0.001, 0.001	
	SD, SE	0.3415, 0.1972	0.0005, 0.0003		0.9222, 0.5324	0.0005, 0.0003	
	MEDIAN	0.842	0.001		1.126	0.001	
	MIN, MAX	0.841, 1.433	0.000, 0.001		0.746, 2.499	0.001, 0.002	
	5%, 95%	0.841, 1.433	0.000, 0.001		0.746, 2.499	0.001, 0.002	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1066	3	4	0.0319
	MEAN, GEO MEAN	1.188, 1.064	0.001, 0.001		1.191, 1.062	0.001, 0.001	
	SD, SE	0.7467, 0.5280	0.0000, 0.0000		0.6187, 0.3572	0.0000, 0.0000	
	MEDIAN	1.188	0.001		1.283	0.001	
	MIN, MAX	0.660, 1.716	0.001, 0.001		0.531, 1.758	0.001, 0.001	
	5%, 95%	0.660, 1.716	0.001, 0.001		0.531, 1.758	0.001, 0.001	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^a	N	3	4	0.0319	3	4	0.0497
	MEAN, GEO MEAN	0.997, 0.939	0.001, 0.001		1.321, 1.176	0.001, 0.001	
	SD, SE	0.4320, 0.2494	0.0000, 0.0000		0.6846, 0.3952	0.0005, 0.0003	
	MEDIAN	0.858	0.001		1.449	0.001	
	MIN, MAX	0.651, 1.481	0.001, 0.001		0.581, 1.932	0.001, 0.002	
	5%, 95%	0.651, 1.481	0.001, 0.001		0.581, 1.932	0.001, 0.002	

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 139 of 264)

Biomarker: Cotinine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.418, 0.383			0.324, 0.277		
	SD, SE	0.1981, 0.1144			0.2214, 0.1278		
	MEDIAN	0.426			0.252		
	MIN, MAX	0.216, 0.612			0.147, 0.572		
	5%, 95%	0.216, 0.612			0.147, 0.572		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.485, 0.439			0.662, 0.543		
	SD, SE	0.2501, 0.1444			0.4289, 0.2476		
	MEDIAN	0.478			0.709		
	MIN, MAX	0.239, 0.739			0.212, 1.066		
	5%, 95%	0.239, 0.739			0.212, 1.066		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.718, 0.712			0.732, 0.467		
	SD, SE	0.1329, 0.0940			0.8125, 0.4691		
	MEDIAN	0.718			0.364		
	MIN, MAX	0.624, 0.812			0.168, 1.663		
	5%, 95%	0.624, 0.812			0.168, 1.663		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.486, 0.437			0.573, 0.458		
	SD, SE	0.2473, 0.1428			0.4096, 0.2365		
	MEDIAN	0.509			0.548		
	MIN, MAX	0.228, 0.721			0.176, 0.994		
	5%, 95%	0.228, 0.721			0.176, 0.994		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 140 of 264)

Biomarker: Cotinine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.074, 0.068			0.057, 0.049		
	SD, SE	0.0350, 0.0202			0.0392, 0.0226		
	MEDIAN	0.075			0.044		
	MIN, MAX	0.038, 0.108			0.026, 0.101		
	5%, 95%	0.038, 0.108			0.026, 0.101		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.085, 0.077			0.117, 0.095		
	SD, SE	0.0440, 0.0254			0.0758, 0.0438		
	MEDIAN	0.084			0.125		
	MIN, MAX	0.042, 0.130			0.037, 0.188		
	5%, 95%	0.042, 0.130			0.037, 0.188		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.127, 0.125			0.129, 0.083		
	SD, SE	0.0233, 0.0165			0.1430, 0.0826		
	MEDIAN	0.127			0.064		
	MIN, MAX	0.110, 0.143			0.030, 0.293		
	5%, 95%	0.110, 0.143			0.030, 0.293		
	# of BLQ/ALQ Values	0/0			0/0		
Overall [*]	N	3		NA	3		NA
	MEAN, GEO MEAN	0.086, 0.077			0.101, 0.081		
	SD, SE	0.0437, 0.0252			0.0721, 0.0416		
	MEDIAN	0.090			0.097		
	MIN, MAX	0.040, 0.127			0.031, 0.175		
	5%, 95%	0.040, 0.127			0.031, 0.175		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439308

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 141 of 264)

Biomarker: Cotinine (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0436	3	3	0.0636
	MEAN, GEO MEAN	6583.8, 5308.2	7.6, 5.0		3693.7, 3619.1	3.1, 3.1	
	SD, SE	4959.84, 2863.57	8.90, 4.45		939.49, 542.41	0.00, 0.00	
	MEDIAN	5463.6	3.1		3338.5	3.1	
	MIN, MAX	2279.8, 12007.9	3.1, 20.9		2983.6, 4759.0	3.1, 3.1	
	5%, 95%	2279.8, 12007.9	3.1, 20.9		2983.6, 4759.0	3.1, 3.1	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0319	3	4	0.0319
	MEAN, GEO MEAN	6439.9, 5581.3	3.1, 3.1		4243.9, 4212.0	3.1, 3.1	
	SD, SE	3631.27, 2096.51	0.00, 0.00		620.20, 358.07	0.00, 0.00	
	MEDIAN	7090.1	3.1		4495.7	3.1	
	MIN, MAX	2527.5, 9702.2	3.1, 3.1		3537.4, 4698.6	3.1, 3.1	
	5%, 95%	2527.5, 9702.2	3.1, 3.1		3537.4, 4698.6	3.1, 3.1	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1066	3	4	0.0319
	MEAN, GEO MEAN	4650.6, 3439.8	3.1, 3.1		3602.1, 3500.7	3.1, 3.1	
	SD, SE	4426.13, 3129.75	0.00, 0.00		1094.83, 632.10	0.00, 0.00	
	MEDIAN	4650.6	3.1		3087.7	3.1	
	MIN, MAX	1520.8, 7780.3	3.1, 3.1		2859.2, 4859.4	3.1, 3.1	
	5%, 95%	1520.8, 7780.3	3.1, 3.1		2859.2, 4859.4	3.1, 3.1	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^a	N	3	4	0.0436	3	4	0.0319
	MEAN, GEO MEAN	6072.1, 5067.8	4.6, 4.0		3846.5, 3787.3	3.1, 3.1	
	SD, SE	3864.42, 2231.12	2.95, 1.48		841.91, 486.07	0.00, 0.00	
	MEDIAN	6276.9	3.1		3640.6	3.1	
	MIN, MAX	2109.4, 9830.1	3.1, 9.0		3126.7, 4772.3	3.1, 3.1	
	5%, 95%	2109.4, 9830.1	3.1, 9.0		3126.7, 4772.3	3.1, 3.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439309

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 142 of 264)

Biomarker: Cotinine (ng/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0436	3	3	0.0636
	MEAN, GEO MEAN	1160.1, 935.3	1.3, 0.8		650.8, 637.7	0.5, 0.5	
	SD, SE	873.93, 504.56	1.60, 0.80		165.53, 95.57	0.00, 0.00	
	MEDIAN	962.7	0.5		588.2	0.5	
	MIN, MAX	401.7, 2115.8	0.5, 3.7		525.7, 838.5	0.5, 0.5	
	5%, 95%	401.7, 2115.8	0.5, 3.7		525.7, 838.5	0.5, 0.5	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Week 2	N	3	4	0.0319	3	4	0.0319
	MEAN, GEO MEAN	1134.7, 983.4	0.5, 0.5		747.8, 742.1	0.5, 0.5	
	SD, SE	639.84, 369.41	0.00, 0.00		109.27, 63.09	0.00, 0.00	
	MEDIAN	1249.3	0.5		792.1	0.5	
	MIN, MAX	445.3, 1709.5	0.5, 0.5		623.3, 827.9	0.5, 0.5	
	5%, 95%	445.3, 1709.5	0.5, 0.5		623.3, 827.9	0.5, 0.5	
	# of BLQ/ALQ Values	0/0	4/0		0/0	4/0	
Week 3	N	2	3	0.1066	3	4	0.0319
	MEAN, GEO MEAN	819.5, 606.1	0.5, 0.5		634.7, 616.8	0.5, 0.5	
	SD, SE	779.87, 551.45	0.00, 0.00		192.88, 111.36	0.00, 0.00	
	MEDIAN	819.5	0.5		544.1	0.5	
	MIN, MAX	268.0, 1370.9	0.5, 0.5		503.8, 856.2	0.5, 0.5	
	5%, 95%	268.0, 1370.9	0.5, 0.5		503.8, 856.2	0.5, 0.5	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	3	4	0.0436	3	4	0.0319
	MEAN, GEO MEAN	1069.9, 893.0	0.8, 0.7		677.8, 667.3	0.5, 0.5	
	SD, SE	680.92, 393.13	0.55, 0.28		148.36, 85.66	0.00, 0.00	
	MEDIAN	1106.0	0.5		641.5	0.5	
	MIN, MAX	371.7, 1732.1	0.5, 1.6		550.9, 840.9	0.5, 0.5	
	5%, 95%	371.7, 1732.1	0.5, 1.6		550.9, 840.9	0.5, 0.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 143 of 264)

Biomarker: Cotinine ((nmol/L)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	539.4, 448.7			159.0, 158.6		
	SD, SE	405.80, 234.29			12.80, 7.39		
	MEDIAN	380.0			165.8		
	MIN, MAX	237.5, 1000.7			144.2, 166.9		
	5%, 95%	237.5, 1000.7			144.2, 166.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	496.4, 429.2			394.9, 314.6		
	SD, SE	337.76, 195.01			337.01, 194.58		
	MEDIAN	354.5			224.8		
	MIN, MAX	252.8, 882.0			176.9, 783.1		
	5%, 95%	252.8, 882.0			176.9, 783.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	451.0, 405.4			374.4, 270.8		
	SD, SE	279.24, 197.45			377.19, 217.77		
	MEDIAN	451.0			158.8		
	MIN, MAX	253.5, 648.4			154.4, 809.9		
	5%, 95%	253.5, 648.4			154.4, 809.9		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	478.4, 419.4			309.4, 260.2		
	SD, SE	316.39, 182.67			233.66, 134.90		
	MEDIAN	296.0			182.0		
	MIN, MAX	295.4, 843.7			167.2, 579.1		
	5%, 95%	295.4, 843.7			167.2, 579.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 144 of 264)

Biomarker: Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	95.1, 79.1			28.0, 27.9		
	SD, SE	71.46, 41.26			2.25, 1.30		
	MEDIAN	67.0			29.2		
	MIN, MAX	41.9, 176.3			25.4, 29.4		
	5%, 95%	41.9, 176.3			25.4, 29.4		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	87.5, 75.6			69.6, 55.5		
	SD, SE	59.52, 34.36			59.38, 34.29		
	MEDIAN	62.5			39.6		
	MIN, MAX	44.5, 155.4			31.2, 138.0		
	5%, 95%	44.5, 155.4			31.2, 138.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	79.5, 71.4			66.0, 47.7		
	SD, SE	49.14, 34.75			66.45, 38.37		
	MEDIAN	79.5			28.0		
	MIN, MAX	44.7, 114.2			27.2, 142.7		
	5%, 95%	44.7, 114.2			27.2, 142.7		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	84.3, 73.9			54.5, 45.9		
	SD, SE	55.69, 32.15			41.13, 23.75		
	MEDIAN	52.2			32.1		
	MIN, MAX	52.1, 148.6			29.5, 102.0		
	5%, 95%	52.1, 148.6			29.5, 102.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 145 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Smokers	Male Non-Smokers	P-value*	Smokers	Female Non-Smokers	P-value*
Week 1	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	13071.938, 6498.188	17.169, 16.468		13773.180, 13119.276	17.412, 15.500	
	SD, SE	11737.0997, 6776.4177	6.0729, 3.5062		5506.3041, 3179.0662	11.2168, 7.9315	
	MEDIAN	14233.849	16.116		10987.230	17.412	
	MIN, MAX	797.096, 24184.869	11.692, 23.700		10216.584, 20115.725	9.480, 25.343	
	5%, 95%	797.096, 24184.869	11.692, 23.700		10216.584, 20115.725	9.480, 25.343	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Week 2	N	3	4	0.0497	3	3	0.0809
	MEAN, GEO MEAN	12636.624, 8989.660	17.795, 17.207		13934.476, 13447.472	19.263, 17.114	
	SD, SE	9131.5180, 5272.0844	5.2448, 2.6224		4577.3678, 2642.7445	9.7891, 5.6517	
	MEDIAN	15906.187	17.499		13037.360	22.713	
	MIN, MAX	2320.420, 19683.264	13.272, 22.910		9872.082, 18893.985	8.216, 26.860	
	5%, 95%	2320.420, 19683.264	13.272, 22.910		9872.082, 18893.985	8.216, 26.860	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	3	0.1489	3	3	0.0809
	MEAN, GEO MEAN	9852.461, 2562.480	17.812, 17.448		11811.580, 11287.298	12.140, 11.974	
	SD, SE	13453.9715, 9513.3945	4.5365, 2.6192		4052.3332, 2339.6156	2.4911, 1.4382	
	MEDIAN	9852.461	16.306		12845.595	11.613	
	MIN, MAX	339.066, 19365.855	14.220, 22.910		7342.419, 15246.725	9.954, 14.852	
	5%, 95%	339.066, 19365.855	14.220, 22.910		7342.419, 15246.725	9.954, 14.852	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Overall*	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	12433.403, 7153.022	17.802, 17.491		13173.078, 12666.849	16.429, 15.218	
	SD, SE	10221.2133, 5901.2203	3.9046, 1.9523		4535.8196, 2618.7567	7.1309, 3.5655	
	MEDIAN	15070.018	16.980		12290.062	16.235	
	MIN, MAX	1152.194, 21077.996	14.536, 22.713		9143.695, 18085.478	9.217, 24.028	
	5%, 95%	1152.194, 21077.996	14.536, 22.713		9143.695, 18085.478	9.217, 24.028	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 146 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	922.373, 549.252			575.506, 574.960		
	SD, SE	977.2890, 564.2381			30.8736, 17.8249		
	MEDIAN	618.863			567.588		
	MIN, MAX	132.849, 2015.406			549.362, 609.567		
	5%, 95%	132.849, 2015.406			549.362, 609.567		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	938.913, 691.198			1431.490, 1004.393		
	SD, SE	788.5418, 455.2648			1489.5090, 859.9684		
	MEDIAN	795.309			651.868		
	MIN, MAX	232.042, 1789.388			493.604, 3148.998		
	5%, 95%	232.042, 1789.388			493.604, 3148.998		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	835.166, 301.991			1197.104, 873.183		
	SD, SE	1101.1845, 778.6550			1169.8366, 675.4055		
	MEDIAN	835.166			642.280		
	MIN, MAX	56.511, 1613.821			407.912, 2541.121		
	5%, 95%	56.511, 1613.821			407.912, 2541.121		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	884.586, 563.990			1068.033, 858.126		
	SD, SE	846.9359, 488.9787			895.7948, 517.1874		
	MEDIAN	707.086			614.503		
	MIN, MAX	140.467, 1806.205			489.701, 2099.895		
	5%, 95%	140.467, 1806.205			489.701, 2099.895		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 147 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	8.559, 4.473	0.009, 0.009		10.895, 10.002	0.019, 0.017	
	SD, SE	8.1809, 4.7232	0.0025, 0.0015		4.8224, 2.7842	0.0092, 0.0065	
	MEDIAN	8.030	0.009		12.975	0.019	
	MIN, MAX	0.656, 16.992	0.007, 0.012		5.382, 14.329	0.012, 0.025	
	5%, 95%	0.656, 16.992	0.007, 0.012		5.382, 14.329	0.012, 0.025	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Week 2	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	10.188, 7.646	0.010, 0.009		10.396, 9.817	0.017, 0.015	
	SD, SE	7.6612, 4.4232	0.0045, 0.0023		3.8935, 2.2479	0.0105, 0.0061	
	MEDIAN	10.399	0.010		11.956	0.017	
	MIN, MAX	2.423, 17.741	0.005, 0.016		5.964, 13.267	0.007, 0.028	
	5%, 95%	2.423, 17.741	0.005, 0.016		5.964, 13.267	0.007, 0.028	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	3	0.1489	3	3	0.0809
	MEAN, GEO MEAN	8.121, 3.076	0.013, 0.013		10.620, 9.613	0.013, 0.012	
	SD, SE	10.6292, 7.5160	0.0038, 0.0022		5.0463, 2.9135	0.0044, 0.0025	
	MEDIAN	8.121	0.015		12.366	0.015	
	MIN, MAX	0.605, 15.637	0.009, 0.016		4.933, 14.562	0.008, 0.016	
	5%, 95%	0.605, 15.637	0.009, 0.016		4.933, 14.562	0.008, 0.016	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	9.078, 5.749	0.011, 0.010		10.637, 9.833	0.017, 0.016	
	SD, SE	7.7819, 4.4929	0.0026, 0.0013		4.5283, 2.6144	0.0059, 0.0030	
	MEDIAN	9.215	0.011		12.869	0.019	
	MIN, MAX	1.228, 16.790	0.007, 0.013		5.426, 13.616	0.009, 0.022	
	5%, 95%	1.228, 16.790	0.007, 0.013		5.426, 13.616	0.009, 0.022	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439315

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 148 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)			Analytical Lab: INBIFO			
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	0.625, 0.378			0.461, 0.438	
	SD, SE	0.6957, 0.4017			0.1765, 0.1019	
	MEDIAN	0.349			0.434	
	MIN, MAX	0.109, 1.416			0.299, 0.649	
	5%, 95%	0.109, 1.416			0.299, 0.649	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	0.792, 0.588			0.985, 0.733	
	SD, SE	0.7247, 0.4184			0.8921, 0.5151	
	MEDIAN	0.520			0.663	
	MIN, MAX	0.242, 1.613			0.298, 1.993	
	5%, 95%	0.242, 1.613			0.298, 1.993	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	0.702, 0.363			1.106, 0.743	
	SD, SE	0.8499, 0.6010			1.1566, 0.6678	
	MEDIAN	0.702			0.618	
	MIN, MAX	0.101, 1.303			0.274, 2.427	
	5%, 95%	0.101, 1.303			0.274, 2.427	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	0.677, 0.456			0.850, 0.671	
	SD, SE	0.6795, 0.3923			0.6878, 0.3971	
	MEDIAN	0.435			0.643	
	MIN, MAX	0.151, 1.444			0.290, 1.618	
	5%, 95%	0.151, 1.444			0.290, 1.618	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 149 of 264)

Biomarker: Cotinine-N-glucuronide (nmol/L)		Analytical Lab: INBJFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	3	0.0636	3	2	0.1386
	MEAN, GEO MEAN	12408.6, 5242.0	7.9, 7.9		6026.8, 5740.5	7.9, 7.9	
	SD, SE	13952.69, 8055.59	0.00, 0.00		2211.40, 1276.75	0.00, 0.00	
	MEDIAN	8840.9	7.9		6081.3	7.9	
	MIN, MAX	586.1, 27798.7	7.9, 7.9		3788.7, 8210.5	7.9, 7.9	
	5%, 95%	586.1, 27798.7	7.9, 7.9		3788.7, 8210.5	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Week 2	N	3	4	0.0319	3	3	0.0636
	MEAN, GEO MEAN	12629.9, 7483.0	7.9, 7.9		5993.1, 5690.5	7.9, 7.9	
	SD, SE	10235.53, 5909.49	0.00, 0.00		2451.58, 1415.42	0.00, 0.00	
	MEDIAN	15442.9	7.9		4985.9	7.9	
	MIN, MAX	1282.0, 21164.8	7.9, 7.9		4205.6, 8787.9	7.9, 7.9	
	5%, 95%	1282.0, 21164.8	7.9, 7.9		4205.6, 8787.9	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	3	0.1066	3	3	0.0636
	MEAN, GEO MEAN	6369.9, 1752.1	7.9, 7.9		5670.4, 5581.6	7.9, 7.9	
	SD, SE	8660.93, 6124.20	0.00, 0.00		1262.84, 729.10	0.00, 0.00	
	MEDIAN	6369.9	7.9		5243.1	7.9	
	MIN, MAX	245.7, 12494.1	7.9, 7.9		4676.7, 7091.5	7.9, 7.9	
	5%, 95%	245.7, 12494.1	7.9, 7.9		4676.7, 7091.5	7.9, 7.9	
	# of BLQ/ALQ Values	0/0	3/0		0/0	3/0	
Overall ^b	N	3	4	0.0319	3	4	0.0319
	MEAN, GEO MEAN	11110.8, 5596.2	7.9, 7.9		5896.8, 5707.7	7.9, 7.9	
	SD, SE	9930.88, 5733.59	0.00, 0.00		1894.02, 1093.51	0.00, 0.00	
	MEDIAN	12141.9	7.9		5248.0	7.9	
	MIN, MAX	704.6, 20485.9	7.9, 7.9		4412.5, 8030.0	7.9, 7.9	
	5%, 95%	704.6, 20485.9	7.9, 7.9		4412.5, 8030.0	7.9, 7.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 150 of 264)

Biomarker: Cotinine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	932.9, 443.1			258.7, 251.6		
	SD, SE	1206.86, 696.78			74.74, 43.15		
	MEDIAN	384.4			248.8		
	MIN, MAX	97.7, 2316.6			189.4, 337.9		
	5%, 95%	97.7, 2316.6			189.4, 337.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	941.5, 575.3			641.4, 425.0		
	SD, SE	909.85, 525.30			713.24, 411.79		
	MEDIAN	772.1			249.3		
	MIN, MAX	128.2, 1924.1			210.3, 1464.7		
	5%, 95%	128.2, 1924.1			210.3, 1464.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	541.1, 206.6			568.0, 431.8		
	SD, SE	707.25, 500.10			531.68, 306.97		
	MEDIAN	541.1			262.2		
	MIN, MAX	41.0, 1041.2			259.8, 1181.9		
	5%, 95%	41.0, 1041.2			259.8, 1181.9		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	809.3, 449.2			489.3, 391.7		
	SD, SE	859.41, 496.18			413.18, 238.55		
	MEDIAN	578.3			282.3		
	MIN, MAX	89.0, 1760.6			220.6, 965.1		
	5%, 95%	89.0, 1760.6			220.6, 965.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 151 of 264)

Biomarker: NNAL (pg/24hr)		Analytical Lab: JNBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	62452.500, 62452.500	11093.333, 10870.393		178820.667, 175395.895	22991.800, 20917.512	
	SD, SE	NA, NA	2584.0041, 1491.8755		41679.4956, 24063.6680	10209.8955, 5104.9478	
	MEDIAN	62452.500	12480.000		185712.000	24310.000	
	MIN, MAX	62452.500, 62452.500	8112.000, 12688.000		134125.000, 216625.000	9984.000, 33363.200	
	5%, 95%	NA, NA	8112.000, 12688.000		134125.000, 216625.000	9984.000, 33363.200	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	105754.000, 105754.000	15461.333, 14181.935		228047.333, 224015.166	23738.000, 23012.947	
	SD, SE	NA, NA	7107.3431, 4103.4264		54220.0312, 31303.9496	6972.0734, 3486.0367	
	MEDIAN	105754.000	16744.000		207101.000	22464.000	
	MIN, MAX	105754.000, 105754.000	7800.000, 21840.000		187425.000, 289616.000	16744.000, 33280.000	
	5%, 95%	NA, NA	7800.000, 21840.000		187425.000, 289616.000	16744.000, 33280.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	84103.250, 84103.250	13277.333, 12618.293		203434.000, 200791.664	23364.900, 22194.160	
	SD, SE	NA, NA	4767.6750, 2752.6185		39131.3891, 22592.5180	8232.4429, 4116.2215	
	MEDIAN	84103.250	14716.000		211863.000	23387.000	
	MIN, MAX	84103.250, 84103.250	7956.000, 17160.000		160775.000, 237664.000	13364.000, 33321.600	
	5%, 95%	NA, NA	7956.000, 17160.000		160775.000, 237664.000	13364.000, 33321.600	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 152 of 264)

Biomarker: NNAL (pmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	298.523, 298.523	53.026, 51.960		854.763, 838.393	109.901, 99.986	
	SD, SE	NA, NA	12.3518, 7.1313		199.2279, 115.0243	48.8031, 24.4015	
	MEDIAN	298.523	59.654		887.703	116.202	
	MIN, MAX	298.523, 298.523	38.775, 60.649		641.118, 1035.468	47.724, 159.476	
	5%, 95%	NA, NA	38.775, 60.649		641.118, 1035.468	47.724, 159.476	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	505.504, 505.504	73.905, 67.790		1090.066, 1070.793	113.468, 110.002	
	SD, SE	NA, NA	33.9730, 19.6143		259.1712, 149.6326	33.3264, 16.6632	
	MEDIAN	505.504	80.036		989.943	107.378	
	MIN, MAX	505.504, 505.504	37.284, 104.395		895.892, 1384.364	80.036, 159.078	
	5%, 95%	NA, NA	37.284, 104.395		895.892, 1384.364	80.036, 159.078	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	402.014, 402.014	63.466, 60.316		972.415, 959.785	111.684, 106.088	
	SD, SE	NA, NA	22.7895, 13.1575		187.0479, 107.9922	39.3510, 19.6755	
	MEDIAN	402.014	70.343		1012.706	111.790	
	MIN, MAX	402.014, 402.014	38.030, 82.025		768.505, 1136.034	63.880, 159.277	
	5%, 95%	NA, NA	38.030, 82.025		768.505, 1136.034	63.880, 159.277	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 153 of 264)

Biomarker: NNAL ((pg/24hr/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	3469.583, 3469.583			12430.719, 11664.330		
	SD, SE	NA, NA			5517.4544, 3185.5038		
	MEDIAN	3469.583			10831.250		
	MIN, MAX	3469.583, 3469.583			7889.706, 18571.200		
	5%, 95%	NA, NA			7889.706, 18571.200		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	5875.222, 5875.222			15171.572, 14019.226		
	SD, SE	NA, NA			7769.4921, 4485.7184		
	MEDIAN	5875.222			11025.000		
	MIN, MAX	5875.222, 5875.222			10355.050, 24134.667		
	5%, 95%	NA, NA			10355.050, 24134.667		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	4672.403, 4672.403			13801.146, 12884.990		
	SD, SE	NA, NA			6564.6507, 3790.1029		
	MEDIAN	4672.403			10593.150		
	MIN, MAX	4672.403, 4672.403			9457.353, 21352.934		
	5%, 95%	NA, NA			9457.353, 21352.934		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 154 of 264)

Biomarker: NNAL ((pmol/24hr)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	16.585, 16.585			59.419, 55.755		
	SD, SE	NA, NA			26.3732, 15.2266		
	MEDIAN	16.585			51.773		
	MIN, MAX	16.585, 16.585			37.713, 88.770		
	5%, 95%	NA, NA			37.713, 88.770		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	28.084, 28.084			72.520, 67.012		
	SD, SE	NA, NA			37.1383, 21.4418		
	MEDIAN	28.084			52.700		
	MIN, MAX	28.084, 28.084			49.497, 115.364		
	5%, 95%	NA, NA			49.497, 115.364		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	22.335, 22.335			65.970, 61.591		
	SD, SE	NA, NA			31.3788, 18.1166		
	MEDIAN	22.335			50.635		
	MIN, MAX	22.335, 22.335			45.207, 102.067		
	5%, 95%	NA, NA			45.207, 102.067		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 155 of 264)

Biomarker: NNAL (pg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	29.054, 29.054	5.550, 5.315		164.779, 140.477	20.888, 17.821	
	SD, SE	NA, NA	1.9500, 1.1258		113.3532, 65.4445	11.5119, 5.7559	
	MEDIAN	29.054	5.462		128.848	22.261	
	MIN, MAX	29.054, 29.054	3.645, 7.542		73.746, 291.743	6.731, 32.298	
	5%, 95%	NA, NA	3.645, 7.542		73.746, 291.743	6.731, 32.298	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	58.056, 58.056	6.737, 6.297		158.882, 148.769	26.820, 23.491	
	SD, SE	NA, NA	2.7931, 1.6126		71.3089, 41.1702	17.2384, 8.6192	
	MEDIAN	58.056	7.202		139.892	20.497	
	MIN, MAX	58.056, 58.056	3.741, 9.269		98.991, 237.764	14.286, 52.000	
	5%, 95%	NA, NA	3.741, 9.269		98.991, 237.764	14.286, 52.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	43.555, 43.555	6.144, 5.814		161.831, 145.379	23.854, 21.132	
	SD, SE	NA, NA	2.3621, 1.3638		92.3086, 53.2944	12.9278, 6.4639	
	MEDIAN	43.555	6.332		134.370	22.483	
	MIN, MAX	43.555, 43.555	3.693, 8.406		86.369, 264.754	10.509, 39.941	
	5%, 95%	NA, NA	3.693, 8.406		86.369, 264.754	10.509, 39.941	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 156 of 264)

Biomarker: NNAL (pmol/mg Creatinine)		Analytical Lab: INBIPO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	0.139, 0.139	0.026, 0.025		0.788, 0.672	0.100, 0.085	
	SD, SE	NA, NA	0.0095, 0.0055		0.5419, 0.3129	0.0549, 0.0274	
	MEDIAN	0.139	0.026		0.616	0.107	
	MIN, MAX	0.139, 0.139	0.017, 0.036		0.353, 1.395	0.032, 0.154	
	5%, 95%	NA, NA	0.017, 0.036		0.353, 1.395	0.032, 0.154	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	0.278, 0.278	0.032, 0.030		0.760, 0.711	0.128, 0.112	
	SD, SE	NA, NA	0.0131, 0.0076		0.3412, 0.1970	0.0826, 0.0413	
	MEDIAN	0.278	0.034		0.669	0.098	
	MIN, MAX	0.278, 0.278	0.018, 0.044		0.473, 1.137	0.068, 0.249	
	5%, 95%	NA, NA	0.018, 0.044		0.473, 1.137	0.068, 0.249	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	0.209, 0.209	0.029, 0.028		0.774, 0.695	0.114, 0.101	
	SD, SE	NA, NA	0.0110, 0.0064		0.4413, 0.2548	0.0618, 0.0309	
	MEDIAN	0.209	0.030		0.643	0.108	
	MIN, MAX	0.209, 0.209	0.018, 0.040		0.413, 1.266	0.050, 0.191	
	5%, 95%	NA, NA	0.018, 0.040		0.413, 1.266	0.050, 0.191	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 157 of 264)

Biomarker: NNAL ((pg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	1.614, 1.614			13.318, 9.342		
	SD, SE	NA, NA			13.7719, 7.9512		
	MEDIAN	1.614			6.442		
	MIN, MAX	1.614, 1.614			4.338, 29.174		
	5%, 95%	NA, NA			4.338, 29.174		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	3.225, 3.225			10.877, 9.310		
	SD, SE	NA, NA			7.7615, 4.4811		
	MEDIAN	3.225			6.995		
	MIN, MAX	3.225, 3.225			5.823, 19.814		
	5%, 95%	NA, NA			5.823, 19.814		
	# of BLQ/ALQ Values	0/0			0/0		
Overall [*]	N	1		NA	3		NA
	MEAN, GEO MEAN	2.420, 2.420			12.098, 9.421		
	SD, SE	NA, NA			10.7664, 6.2160		
	MEDIAN	2.420			6.719		
	MIN, MAX	2.420, 2.420			5.081, 24.494		
	5%, 95%	NA, NA			5.081, 24.494		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 158 of 264)

Biomarker: NNAL ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	0.008, 0.008			0.064, 0.043		
	SD, SE	NA, NA			0.0660, 0.0381		
	MEDIAN	0.008			0.031		
	MIN, MAX	0.008, 0.008			0.021, 0.140		
	5%, 95%	NA, NA			0.021, 0.140		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	0.015, 0.015			0.052, 0.044		
	SD, SE	NA, NA			0.0373, 0.0215		
	MEDIAN	0.015			0.033		
	MIN, MAX	0.015, 0.015			0.028, 0.095		
	5%, 95%	NA, NA			0.028, 0.095		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	0.012, 0.012			0.058, 0.046		
	SD, SE	NA, NA			0.0518, 0.0299		
	MEDIAN	0.012			0.032		
	MIN, MAX	0.012, 0.012			0.025, 0.118		
	5%, 95%	NA, NA			0.025, 0.118		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 159 of 264)

Biomarker: NNAL (pg/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	83.3, 83.3	10.4, 10.4		135.9, 133.2	10.4, 10.4	
	SD, SE	NA, NA	0.00, 0.00		33.86, 19.55	0.00, 0.00	
	MEDIAN	83.3	10.4		127.2	10.4	
	MIN, MAX	83.3, 83.3	10.4, 10.4		107.3, 173.3	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 10.4		107.3, 173.3	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	46.0, 46.0	10.4, 10.4		189.5, 178.6	10.4, 10.4	
	SD, SE	NA, NA	0.00, 0.00		82.91, 47.87	0.00, 0.00	
	MEDIAN	46.0	10.4		157.4	10.4	
	MIN, MAX	46.0, 46.0	10.4, 10.4		127.5, 283.7	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 10.4		127.5, 283.7	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	64.7, 64.7	10.4, 10.4		162.7, 156.3	10.4, 10.4	
	SD, SE	NA, NA	0.00, 0.00		58.30, 33.66	0.00, 0.00	
	MEDIAN	64.7	10.4		142.3	10.4	
	MIN, MAX	64.7, 64.7	10.4, 10.4		117.4, 228.5	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 10.4		117.4, 228.5	10.4, 10.4	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 160 of 264)

Biomarker: NNAL (pmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	398.2, 398.2	49.7, 49.7		649.8, 636.9	49.7, 49.7	
	SD, SE	NA, NA	0.00, 0.00		161.84, 93.44	0.00, 0.00	
	MEDIAN	398.2	49.7		608.0	49.7	
	MIN, MAX	398.2, 398.2	49.7, 49.7		512.9, 828.4	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 49.7		512.9, 828.4	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	219.9, 219.9	49.7, 49.7		906.0, 853.6	49.7, 49.7	
	SD, SE	NA, NA	0.00, 0.00		396.29, 228.80	0.00, 0.00	
	MEDIAN	219.9	49.7		752.4	49.7	
	MIN, MAX	219.9, 219.9	49.7, 49.7		609.5, 1356.1	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 49.7		609.5, 1356.1	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	309.1, 309.1	49.7, 49.7		777.9, 747.1	49.7, 49.7	
	SD, SE	NA, NA	0.00, 0.00		278.70, 160.91	0.00, 0.00	
	MEDIAN	309.1	49.7		680.2	49.7	
	MIN, MAX	309.1, 309.1	49.7, 49.7		561.2, 1092.3	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 49.7		561.2, 1092.3	49.7, 49.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 161 of 264)

Biomarker: NNAL (pg/mL/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	4.6, 4.6			9.2, 8.9		
	SD, SE	NA, NA			3.23, 1.87		
	MEDIAN	4.6			8.7		
	MIN, MAX	4.6, 4.6			6.3, 12.7		
	5%, 95%	NA, NA			6.3, 12.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	2.6, 2.6			11.6, 11.2		
	SD, SE	NA, NA			3.59, 2.07		
	MEDIAN	2.6			13.1		
	MIN, MAX	2.6, 2.6			7.5, 14.2		
	5%, 95%	NA, NA			7.5, 14.2		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	3.6, 3.6			10.4, 10.1		
	SD, SE	NA, NA			3.14, 1.81		
	MEDIAN	3.6			11.5		
	MIN, MAX	3.6, 3.6			6.9, 12.9		
	5%, 95%	NA, NA			6.9, 12.9		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 162 of 264)

Biomarker: NNAL ((pmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	22.1, 22.1			44.1, 42.4		
	SD, SE	NA, NA			15.48, 8.94		
	MEDIAN	22.1			41.4		
	MIN, MAX	22.1, 22.1			30.2, 60.8		
	5%, 95%	NA, NA			30.2, 60.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	12.2, 12.2			55.5, 53.4		
	SD, SE	NA, NA			17.14, 9.89		
	MEDIAN	12.2			62.7		
	MIN, MAX	12.2, 12.2			35.9, 67.8		
	5%, 95%	NA, NA			35.9, 67.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	17.2, 17.2			49.8, 48.2		
	SD, SE	NA, NA			14.93, 8.62		
	MEDIAN	17.2			54.6		
	MIN, MAX	17.2, 17.2			33.1, 61.8		
	5%, 95%	NA, NA			33.1, 61.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 163 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	152850.000, 152850.000	11093.333, 10870.393		681789.333, 669555.039	22991.800, 20917.512	
	SD, SE	NA, NA	2584.0041, 1491.8755		156190.6096, 90176.6905	10209.8955, 5104.9478	
	MEDIAN	152850.000	12480.000		686875.000	24310.000	
	MIN, MAX	152850.000, 152850.000	8112.000, 12688.000		523118.000, 835375.000	9984.000, 33363.200	
	5%, 95%	NA, NA	8112.000, 12688.000		523118.000, 835375.000	9984.000, 33363.200	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	413080.000, 413080.000	23536.500, 19211.985		642731.000, 634249.181	23738.000, 23012.947	
	SD, SE	NA, NA	17161.2786, 8580.6393		132354.3168, 76414.8004	6972.0734, 3486.0367	
	MEDIAN	413080.000	19292.000		571809.000	22464.000	
	MIN, MAX	413080.000, 413080.000	7800.000, 47762.000		560952.000, 795432.000	16744.000, 33280.000	
	5%, 95%	NA, NA	7800.000, 47762.000		560952.000, 795432.000	16744.000, 33280.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	282965.000, 282965.000	21898.500, 17600.341		662260.167, 661662.957	23364.900, 22194.160	
	SD, SE	NA, NA	17676.3083, 8838.1542		34507.7257, 19923.0447	8232.4429, 4116.2215	
	MEDIAN	282965.000	15938.000		659275.000	23387.000	
	MIN, MAX	282965.000, 282965.000	7956.000, 47762.000		629342.000, 698163.500	13364.000, 33321.600	
	5%, 95%	NA, NA	7956.000, 47762.000		629342.000, 698163.500	13364.000, 33321.600	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 164 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	730.623, 730.623	53.026, 51.960		3258.953, 3200.473	109.901, 99.986	
	SD, SE	NA, NA	12.3518, 7.1313		746.5914, 431.0447	48.8031, 24.4015	
	MEDIAN	730.623	59.654		3283.263	116.202	
	MIN, MAX	730.623, 730.623	38.775, 60.649		2500.504, 3993.093	47.724, 159.476	
	5%, 95%	NA, NA	38.775, 60.649		2500.504, 3993.093	47.724, 159.476	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	1974.522, 1974.522	112.504, 91.833		3072.254, 3031.711	113.468, 110.002	
	SD, SE	NA, NA	82.0308, 41.0154		632.6535, 365.2627	33.3264, 16.6632	
	MEDIAN	1974.522	92.216		2733.247	107.378	
	MIN, MAX	1974.522, 1974.522	37.284, 228.302		2681.351, 3802.165	80.036, 159.078	
	5%, 95%	NA, NA	37.284, 228.302		2681.351, 3802.165	80.036, 159.078	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall*	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	1352.573, 1352.573	104.675, 84.130		3165.604, 3162.749	111.684, 106.088	
	SD, SE	NA, NA	84.4924, 42.2462		164.9470, 95.2322	39.3510, 19.6755	
	MEDIAN	1352.573	76.184		3151.335	111.790	
	MIN, MAX	1352.573, 1352.573	38.030, 228.302		3008.255, 3337.222	63.880, 159.277	
	5%, 95%	NA, NA	38.030, 228.302		3008.255, 3337.222	63.880, 159.277	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 165 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	8491.667, 8491.667			45265.085, 44527.329		
	SD, SE	NA, NA			9590.2148, 5536.9131		
	MEDIAN	8491.667			49139.706		
	MIN, MAX	8491.667, 8491.667			34343.750, 52311.800		
	5%, 95%	NA, NA			34343.750, 52311.800		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	22948.889, 22948.889			42624.542, 39692.324		
	SD, SE	NA, NA			20609.5428, 11898.9251		
	MEDIAN	22948.889			32997.176		
	MIN, MAX	22948.889, 22948.889			28590.450, 66286.000		
	5%, 95%	NA, NA			28590.450, 66286.000		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	15720.278, 15720.278			43944.814, 42475.372		
	SD, SE	NA, NA			14137.0935, 8162.0547		
	MEDIAN	15720.278			41068.441		
	MIN, MAX	15720.278, 15720.278			31467.100, 59298.900		
	5%, 95%	NA, NA			31467.100, 59298.900		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 166 of 264)

Biomarker: NNAL plus NNAL-gluc ((pmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	40.590, 40.590			216.367, 212.841		
	SD, SE	NA, NA			45.8412, 26.4664		
	MEDIAN	40.590			234.888		
	MIN, MAX	40.590, 40.590			164.163, 250.050		
	5%, 95%	NA, NA			164.163, 250.050		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	109.696, 109.696			203.745, 189.729		
	SD, SE	NA, NA			98.5136, 56.8768		
	MEDIAN	109.696			157.727		
	MIN, MAX	109.696, 109.696			136.662, 316.847		
	5%, 95%	NA, NA			136.662, 316.847		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	75.143, 75.143			210.057, 203.033		
	SD, SE	NA, NA			67.5752, 39.0146		
	MEDIAN	75.143			196.308		
	MIN, MAX	75.143, 75.143			150.413, 283.449		
	5%, 95%	NA, NA			150.413, 283.449		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 167 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	71.110, 71.110	5.550, 5.315		563.217, 536.255	20.888, 17.821	
	SD, SE	NA, NA	1.9500, 1.1258		225.3635, 130.1137	11.5119, 5.7559	
	MEDIAN	71.110	5.462		459.313	22.261	
	MIN, MAX	71.110, 71.110	3.645, 7.542		408.550, 821.789	6.731, 32.298	
	5%, 95%	NA, NA	3.645, 7.542		408.550, 821.789	6.731, 32.298	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	226.768, 226.768	11.728, 9.037		445.179, 421.205	26.820, 23.491	
	SD, SE	NA, NA	10.2390, 5.1195		185.5327, 107.1173	17.2384, 8.6192	
	MEDIAN	226.768	8.236		386.243	20.497	
	MIN, MAX	226.768, 226.768	3.741, 26.701		296.273, 653.021	14.286, 52.000	
	5%, 95%	NA, NA	3.741, 26.701		296.273, 653.021	14.286, 52.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall*	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	148.939, 148.939	11.283, 8.512		504.198, 480.170	23.854, 21.132	
	SD, SE	NA, NA	10.4580, 5.2290		202.2006, 116.7406	12.9278, 6.4639	
	MEDIAN	148.939	7.369		397.397	22.483	
	MIN, MAX	148.939, 148.939	3.693, 26.701		377.793, 737.405	10.509, 39.941	
	5%, 95%	NA, NA	3.693, 26.701		377.793, 737.405	10.509, 39.941	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 168 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0518
	MEAN, GEO MEAN	0.340, 0.340	0.026, 0.025		2.692, 2.564	0.100, 0.085	
	SD, SE	NA, NA	0.0095, 0.0055		1.0770, 0.6218	0.0549, 0.0274	
	MEDIAN	0.340	0.026		2.196	0.107	
	MIN, MAX	0.340, 0.340	0.017, 0.036		1.953, 3.928	0.032, 0.154	
	5%, 95%	NA, NA	0.017, 0.036		1.953, 3.928	0.032, 0.154	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	1.084, 1.084	0.056, 0.043		2.128, 2.013	0.128, 0.112	
	SD, SE	NA, NA	0.0492, 0.0246		0.8867, 0.5119	0.0826, 0.0413	
	MEDIAN	1.084	0.039		1.846	0.098	
	MIN, MAX	1.084, 1.084	0.018, 0.128		1.416, 3.121	0.068, 0.249	
	5%, 95%	NA, NA	0.018, 0.128		1.416, 3.121	0.068, 0.249	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	4	NA	3	4	0.0518
	MEAN, GEO MEAN	0.712, 0.712	0.054, 0.041		2.410, 2.295	0.114, 0.101	
	SD, SE	NA, NA	0.0501, 0.0251		0.9665, 0.5580	0.0618, 0.0309	
	MEDIAN	0.712	0.035		1.900	0.108	
	MIN, MAX	0.712, 0.712	0.018, 0.128		1.806, 3.525	0.050, 0.191	
	5%, 95%	NA, NA	0.018, 0.128		1.806, 3.525	0.050, 0.191	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 169 of 264)

Biomarker: NNAL plus NNAL-gluc ((pg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	3.951, 3.951			43.208, 35.663		
	SD, SE	NA, NA			33.9101, 19.5780		
	MEDIAN	3.951			27.018		
	MIN, MAX	3.951, 3.951			20.428, 82.179		
	5%, 95%	NA, NA			20.428, 82.179		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	12.598, 12.598			30.386, 26.360		
	SD, SE	NA, NA			20.8336, 12.0283		
	MEDIAN	12.598			19.312		
	MIN, MAX	12.598, 12.598			17.428, 54.418		
	5%, 95%	NA, NA			17.428, 54.418		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	8.275, 8.275			36.797, 31.127		
	SD, SE	NA, NA			27.3066, 15.7655		
	MEDIAN	8.275			22.223		
	MIN, MAX	8.275, 8.275			19.870, 68.299		
	5%, 95%	NA, NA			19.870, 68.299		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 170 of 264)

Biomarker: NNAL plus NNAL-gluc ((pmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	0.019, 0.019			0.207, 0.171		
	SD, SE	NA, NA			0.1621, 0.0936		
	MEDIAN	0.019			0.129		
	MIN, MAX	0.019, 0.019			0.098, 0.393		
	5%, 95%	NA, NA			0.098, 0.393		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	0.060, 0.060			0.145, 0.126		
	SD, SE	NA, NA			0.0997, 0.0576		
	MEDIAN	0.060			0.092		
	MIN, MAX	0.060, 0.060			0.083, 0.260		
	5%, 95%	NA, NA			0.083, 0.260		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	0.040, 0.040			0.176, 0.149		
	SD, SE	NA, NA			0.1309, 0.0756		
	MEDIAN	0.040			0.106		
	MIN, MAX	0.040, 0.040			0.095, 0.327		
	5%, 95%	NA, NA			0.095, 0.327		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 171 of 264)

Biomarker: NNAL plus NNAL-gluc (pg/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	203.8, 203.8	10.4, 10.4		525.4, 508.6	10.4, 10.4	
	SD, SE	NA, NA	0.00, 0.00		156.40, 90.30	0.00, 0.00	
	MEDIAN	203.8	10.4		549.5	10.4	
	MIN, MAX	203.8, 203.8	10.4, 10.4		358.3, 668.3	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 10.4		358.3, 668.3	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0319
	MEAN, GEO MEAN	179.6, 179.6	17.0, 14.3		532.4, 505.6	10.4, 10.4	
	SD, SE	NA, NA	13.15, 6.58		218.76, 126.30	0.00, 0.00	
	MEDIAN	179.6	10.4		432.3	10.4	
	MIN, MAX	179.6, 179.6	10.4, 36.7		381.6, 783.3	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 36.7		381.6, 783.3	10.4, 10.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	4	NA	3	4	0.0319
	MEAN, GEO MEAN	191.7, 191.7	17.0, 14.3		528.9, 517.1	10.4, 10.4	
	SD, SE	NA, NA	13.15, 6.58		135.59, 78.28	0.00, 0.00	
	MEDIAN	191.7	10.4		525.0	10.4	
	MIN, MAX	191.7, 191.7	10.4, 36.7		395.3, 666.4	10.4, 10.4	
	5%, 95%	NA, NA	10.4, 36.7		395.3, 666.4	10.4, 10.4	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 172 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	974.2, 974.2	49.7, 49.7		2511.3, 2431.2	49.7, 49.7	
	SD, SE	NA, NA	0.00, 0.00		747.60, 431.63	0.00, 0.00	
	MEDIAN	974.2	49.7		2626.6	49.7	
	MIN, MAX	974.2, 974.2	49.7, 49.7		1712.7, 3194.5	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 49.7		1712.7, 3194.5	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	4	NA	3	4	0.0319
	MEAN, GEO MEAN	858.5, 858.5	81.1, 68.1		2544.9, 2416.6	49.7, 49.7	
	SD, SE	NA, NA	62.85, 31.43		1045.70, 603.74	0.00, 0.00	
	MEDIAN	858.5	49.7		2066.4	49.7	
	MIN, MAX	858.5, 858.5	49.7, 175.4		1824.0, 3744.2	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 175.4		1824.0, 3744.2	49.7, 49.7	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	4	NA	3	4	0.0319
	MEAN, GEO MEAN	916.4, 916.4	81.1, 68.1		2528.1, 2471.9	49.7, 49.7	
	SD, SE	NA, NA	62.85, 31.43		648.10, 374.18	0.00, 0.00	
	MEDIAN	916.4	49.7		2509.3	49.7	
	MIN, MAX	916.4, 916.4	49.7, 175.4		1889.6, 3185.4	49.7, 49.7	
	5%, 95%	NA, NA	49.7, 175.4		1889.6, 3185.4	49.7, 49.7	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: NNAL plus NNAL-gluc ((pg/mL)/cigarette per day)			Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Male		Female	
			Non-Smokers	P-value ^a	Non-Smokers	P-value ^a
Week 1	N	1		NA	3	NA
	MEAN, GEO MEAN	11.3, 11.3			34.2, 33.8	
	SD, SE	NA, NA			6.06, 3.50	
	MEDIAN	11.3			35.8	
	MIN, MAX	11.3, 11.3			27.5, 39.3	
	5%, 95%	NA, NA			27.5, 39.3	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	1		NA	3	NA
	MEAN, GEO MEAN	10.0, 10.0			32.5, 31.6	
	SD, SE	NA, NA			8.92, 5.15	
	MEDIAN	10.0			36.0	
	MIN, MAX	10.0, 10.0			22.4, 39.2	
	5%, 95%	NA, NA			22.4, 39.2	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	1		NA	3	NA
	MEAN, GEO MEAN	10.7, 10.7			33.4, 33.3	
	SD, SE	NA, NA			2.50, 1.44	
	MEDIAN	10.7			33.4	
	MIN, MAX	10.7, 10.7			30.9, 35.9	
	5%, 95%	NA, NA			30.9, 35.9	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 174 of 264)

Biomarker: NNAL plus NNAL-gluc (pmol/L/cigarette per day)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male			Female	
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers
Week 1	N	1		NA	3	NA
	MEAN, GEO MEAN	54.1, 54.1			163.5, 161.7	
	SD, SE	NA, NA			29.10, 16.80	
	MEDIAN	54.1			171.3	
	MIN, MAX	54.1, 54.1			131.3, 187.9	
	5%, 95%	NA, NA			131.3, 187.9	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	1		NA	3	NA
	MEAN, GEO MEAN	47.7, 47.7			155.6, 151.2	
	SD, SE	NA, NA			42.47, 24.52	
	MEDIAN	47.7			172.2	
	MIN, MAX	47.7, 47.7			107.3, 187.2	
	5%, 95%	NA, NA			107.3, 187.2	
	# of BLQ/ALQ Values	0/0			0/0	
Overall [*]	N	1		NA	3	NA
	MEAN, GEO MEAN	50.9, 50.9			159.6, 159.3	
	SD, SE	NA, NA			12.10, 6.99	
	MEDIAN	50.9			159.3	
	MIN, MAX	50.9, 50.9			147.6, 171.8	
	5%, 95%	NA, NA			147.6, 171.8	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 175 of 264)

Biomarker: NNAL-O-glucuronide (pmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	576.1, 576.1	0.0, NA		1861.5, 1746.5	0.0, NA	
	SD, SE	NA, NA	0.00, 0.00		790.35, 456.31	0.00, 0.00	
	MEDIAN	576.1	0.0		1798.2	0.0	
	MIN, MAX	576.1, 576.1	0.0, 0.0		1104.7, 2681.6	0.0, 0.0	
	5%, 95%	NA, NA	0.0, 0.0		1104.7, 2681.6	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	638.7, 638.7	0.0, NA		1638.9, 1562.0	0.0, NA	
	SD, SE	NA, NA	0.00, 0.00		650.73, 375.70	0.00, 0.00	
	MEDIAN	638.7	0.0		1314.0	0.0	
	MIN, MAX	638.7, 638.7	0.0, 0.0		1214.6, 2388.1	0.0, 0.0	
	5%, 95%	NA, NA	0.0, 0.0		1214.6, 2388.1	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	607.4, 607.4	0.0, NA		1750.2, 1702.1	0.0, NA	
	SD, SE	NA, NA	0.00, 0.00		473.96, 273.64	0.00, 0.00	
	MEDIAN	607.4	0.0		1948.1	0.0	
	MIN, MAX	607.4, 607.4	0.0, 0.0		1209.4, 2093.2	0.0, 0.0	
	5%, 95%	NA, NA	0.0, 0.0		1209.4, 2093.2	0.0, 0.0	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 176 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/L)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	32.0, 32.0			119.4, 116.1		
	SD, SE	NA, NA			34.76, 20.07		
	MEDIAN	32.0			110.5		
	MIN, MAX	32.0, 32.0			89.9, 157.7		
	5%, 95%	NA, NA			89.9, 157.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	35.5, 35.5			100.1, 97.7		
	SD, SE	NA, NA			25.34, 14.63		
	MEDIAN	35.5			109.5		
	MIN, MAX	35.5, 35.5			71.4, 119.4		
	5%, 95%	NA, NA			71.4, 119.4		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	33.8, 33.8			109.8, 109.7		
	SD, SE	NA, NA			4.95, 2.86		
	MEDIAN	33.8			110.0		
	MIN, MAX	33.8, 33.8			104.7, 114.6		
	5%, 95%	NA, NA			104.7, 114.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance-CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 177 of 264)

Biomarker: NNAL-O-glucuronide (pmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	432.075, 432.075	0.000, NA		2404.204, 2299.057	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		880.0617, 508.1039	0.0000, 0.0000	
	MEDIAN	432.075	0.000		2247.750	0.000	
	MIN, MAX	432.075, 432.075	0.000, 0.000		1612.862, 3352.000	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		1612.862, 3352.000	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	1469.010, 1469.010	0.000, NA		1982.178, 1959.655	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		377.8130, 218.1304	0.0000, 0.0000	
	MEDIAN	1469.010	0.000		1785.462	0.000	
	MIN, MAX	1469.010, 1469.010	0.000, 0.000		1743.313, 2417.760	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		1743.313, 2417.760	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall ^b	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	950.543, 950.543	0.000, NA		2193.191, 2177.909	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		325.3772, 187.8566	0.0000, 0.0000	
	MEDIAN	950.543	0.000		2015.311	0.000	
	MIN, MAX	950.543, 950.543	0.000, 0.000		1995.532, 2568.731	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		1995.532, 2568.731	0.000, 0.000	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 178 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	24.004, 24.004			156.950, 152.894		
	SD, SE	NA, NA			42.5600, 24.5720		
	MEDIAN	24.004			151.286		
	MIN, MAX	24.004, 24.004			112.388, 197.176		
	5%, 95%	NA, NA			112.388, 197.176		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	81.612, 81.612			131.224, 122.638		
	SD, SE	NA, NA			61.4951, 35.5042		
	MEDIAN	81.612			105.027		
	MIN, MAX	81.612, 81.612			87.166, 201.480		
	5%, 95%	NA, NA			87.166, 201.480		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	52.808, 52.808			144.087, 139.840		
	SD, SE	NA, NA			41.2527, 23.8173		
	MEDIAN	52.808			151.102		
	MIN, MAX	52.808, 52.808			99.777, 181.383		
	5%, 95%	NA, NA			99.777, 181.383		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 179 of 264)

Biomarker: NNAL-O-glucuronide (pmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	0.201, 0.201	0.000, NA		1.905, 1.841	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		0.6009, 0.3469	0.0000, 0.0000	
	MEDIAN	0.201	0.000		1.843	0.000	
	MIN, MAX	0.201, 0.201	0.000, 0.000		1.337, 2.534	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		1.337, 2.534	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Week 3	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	0.806, 0.806	0.000, NA		1.369, 1.302	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		0.5465, 0.3155	0.0000, 0.0000	
	MEDIAN	0.806	0.000		1.178	0.000	
	MIN, MAX	0.806, 0.806	0.000, 0.000		0.943, 1.985	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		0.943, 1.985	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	3/0		0/0	4/0	
Overall*	N	1	3	NA	3	4	0.0319
	MEAN, GEO MEAN	0.504, 0.504	0.000, NA		1.637, 1.582	0.000, NA	
	SD, SE	NA, NA	0.0000, 0.0000		0.5437, 0.3139	0.0000, 0.0000	
	MEDIAN	0.504	0.000		1.393	0.000	
	MIN, MAX	0.504, 0.504	0.000, 0.000		1.258, 2.260	0.000, 0.000	
	5%, 95%	NA, NA	0.000, 0.000		1.258, 2.260	0.000, 0.000	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 180 of 264)

Biomarker: NNAL-O-glucuronide ((pmol/mg Creatinine)/cigarette per day). Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	1		NA	3		NA
	MEAN, GEO MEAN	0.011, 0.011			0.143, 0.122		
	SD, SE	NA, NA			0.0977, 0.0564		
	MEDIAN	0.011			0.108		
	MIN, MAX	0.011, 0.011			0.067, 0.253		
	5%, 95%	NA, NA			0.067, 0.253		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	1		NA	3		NA
	MEAN, GEO MEAN	0.045, 0.045			0.093, 0.081		
	SD, SE	NA, NA			0.0624, 0.0360		
	MEDIAN	0.045			0.059		
	MIN, MAX	0.045, 0.045			0.055, 0.165		
	5%, 95%	NA, NA			0.055, 0.165		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	1		NA	3		NA
	MEAN, GEO MEAN	0.028, 0.028			0.118, 0.103		
	SD, SE	NA, NA			0.0794, 0.0458		
	MEDIAN	0.028			0.082		
	MIN, MAX	0.028, 0.028			0.063, 0.209		
	5%, 95%	NA, NA			0.063, 0.209		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 181 of 264)

Biomarker: Nicotine (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	1	NA
	MEAN, GEO MEAN	14331.711, 12198.457	8.568, 8.411		4905.957, 4586.575	4.080, 4.080	
	SD, SE	8085.8497, 4668.3675	2.3080, 1.6320		2292.4115, 1323.5244	NA, NA	
	MEDIAN	18042.756	8.568		3934.140	4.080	
	MIN, MAX	5056.480, 19895.897	6.936, 10.200		3259.536, 7524.195	4.080, 4.080	
	5%, 95%	5056.480, 19895.897	6.936, 10.200		3259.536, 7524.195	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	9324.814, 8030.613			7091.661, 6235.018	7.548, 6.393	
	SD, SE	5185.5625, 2993.8859			4448.8210, 2568.5280	5.6738, 4.0120	
	MEDIAN	11101.546			5608.210	7.548	
	MIN, MAX	3484.431, 13388.466			3574.098, 12092.675	3.536, 11.560	
	5%, 95%	3484.431, 13388.466			3574.098, 12092.675	3.536, 11.560	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2453	3	2	0.1489
	MEAN, GEO MEAN	5166.295, 4177.408	6.569, 6.554		6564.503, 6173.722	7.582, 6.827	
	SD, SE	4298.8062, 3039.7150	0.6350, 0.4490		2592.1298, 1496.5668	4.6641, 3.2980	
	MEDIAN	5166.295	6.569		7103.308	7.582	
	MIN, MAX	2126.580, 8206.010	6.120, 7.018		3745.315, 8844.885	4.284, 10.880	
	5%, 95%	2126.580, 8206.010	6.120, 7.018		3745.315, 8844.885	4.284, 10.880	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	10755.654, 8996.488	7.915, 7.760		6187.374, 5801.024	8.802, 7.931	
	SD, SE	6339.1567, 3659.9138	1.9937, 1.1511		2859.8265, 1651.1216	4.2013, 2.4256	
	MEDIAN	13212.411	7.018		4645.647	10.880	
	MIN, MAX	3555.830, 15498.722	6.528, 10.200		4429.222, 9487.252	3.967, 11.560	
	5%, 95%	3555.830, 15498.722	6.528, 10.200		4429.222, 9487.252	3.967, 11.560	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 182 of 264)

Biomarker: Nicotine (µg/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	3	2	0.1489	3	1	NA
	MEAN, GEO MEAN	2324.603, 1978.590	1.390, 1.364		795.746, 743.943	0.662, 0.662	
	SD, SE	1311.5247, 757.2091	0.3741, 0.2645		371.8287, 214.6754	NA, NA	
	MEDIAN	2926.535	1.390		638.118	0.662	
	MIN, MAX	820.161, 3227.114	1.125, 1.654		528.697, 1220.424	0.662, 0.662	
	5%, 95%	820.161, 3227.114	1.125, 1.654		528.697, 1220.424	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	1512.485, 1302.566			1150.268, 1011.320	1.225, 1.037	
	SD, SE	841.0980, 485.6082			721.5987, 416.6152	0.9199, 0.6505	
	MEDIAN	1800.671			909.652	1.225	
	MIN, MAX	565.175, 2171.609			579.719, 1961.432	0.574, 1.875	
	5%, 95%	565.175, 2171.609			579.719, 1961.432	0.574, 1.875	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2453	3	2	0.1489
	MEAN, GEO MEAN	837.973, 677.575	1.066, 1.063		1064.762, 1001.378	1.230, 1.108	
	SD, SE	697.2667, 493.0420	0.1025, 0.0725		420.4434, 242.7431	0.7566, 0.5350	
	MEDIAN	837.973	1.066		1152.157	1.230	
	MIN, MAX	344.931, 1331.015	0.993, 1.138		607.490, 1434.640	0.695, 1.765	
	5%, 95%	344.931, 1331.015	0.993, 1.138		607.490, 1434.640	0.695, 1.765	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall*	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	1744.567, 1459.231	1.284, 1.259		1003.592, 940.926	1.428, 1.287	
	SD, SE	1028.2111, 593.6380	0.3231, 0.1866		463.8636, 267.8118	0.6812, 0.3933	
	MEDIAN	2143.053	1.138		753.524	1.765	
	MIN, MAX	576.756, 2513.893	1.059, 1.654		718.420, 1538.832	0.644, 1.875	
	5%, 95%	576.756, 2513.893	1.059, 1.654		718.420, 1538.832	0.644, 1.875	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 183 of 264)

Biomarker: Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1070.450, 1031.062			201.933, 201.009		
	SD, SE	375.2527, 216.6523			23.8930, 13.7946		
	MEDIAN	865.039			196.707		
	MIN, MAX	842.747, 1503.563			181.085, 228.006		
	5%, 95%	842.747, 1503.563			181.085, 228.006		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	706.884, 617.458			824.854, 465.694		
	SD, SE	453.8058, 262.0049			1032.3362, 596.0196		
	MEDIAN	555.077			280.411		
	MIN, MAX	348.443, 1217.133			178.705, 2015.446		
	5%, 95%	348.443, 1217.133			178.705, 2015.446		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	519.132, 492.312			685.347, 477.598		
	SD, SE	232.9238, 164.7020			690.9447, 398.9171		
	MEDIAN	519.132			394.628		
	MIN, MAX	354.430, 683.834			187.266, 1474.148		
	5%, 95%	354.430, 683.834			187.266, 1474.148		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	786.703, 745.997			570.711, 410.182		
	SD, SE	316.8485, 182.9326			579.1226, 334.3566		
	MEDIAN	710.058			251.473		
	MIN, MAX	515.207, 1134.843			221.461, 1239.200		
	5%, 95%	515.207, 1134.843			221.461, 1239.200		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Nicotine ((ug/24hr)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	173.627, 167.238			32.754, 32.604		
	SD, SE	60.8660, 35.1410			3.8757, 2.2376		
	MEDIAN	140.309			31.906		
	MIN, MAX	136.694, 243.878			29.372, 36.983		
	5%, 95%	136.694, 243.878			29.372, 36.983		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	114.657, 100.152			133.791, 75.536		
	SD, SE	73.6070, 42.4970			167.4446, 96.6742		
	MEDIAN	90.034			45.483		
	MIN, MAX	56.518, 197.419			28.986, 326.905		
	5%, 95%	56.518, 197.419			28.986, 326.905		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	84.204, 79.853			111.164, 77.467		
	SD, SE	37.7800, 26.7145			112.0711, 64.7043		
	MEDIAN	84.204			64.009		
	MIN, MAX	57.489, 110.918			30.375, 239.107		
	5%, 95%	57.489, 110.918			30.375, 239.107		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	127.604, 121.001			92.569, 66.532		
	SD, SE	51.3928, 29.6717			93.9335, 54.2325		
	MEDIAN	115.172			40.789		
	MIN, MAX	83.567, 184.072			35.921, 200.998		
	5%, 95%	83.567, 184.072			35.921, 200.998		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 185 of 264)

Biomarker: Nicotine (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	1	NA
	MEAN, GEO MEAN	9.355, 8.398	0.005, 0.004		3.908, 3.497	0.005, 0.005	
	SD, SE	4.5544, 2.6295	0.0007, 0.0005		1.9305, 1.1146	NA, NA	
	MEDIAN	11.224	0.005		4.646	0.005	
	MIN, MAX	4.163, 12.677	0.004, 0.005		1.717, 5.360	0.005, 0.005	
	5%, 95%	4.163, 12.677	0.004, 0.005		1.717, 5.360	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	7.655, 6.831			5.173, 4.551	0.008, 0.006	
	SD, SE	4.2280, 2.4410			2.7852, 1.6080	0.0064, 0.0045	
	MEDIAN	7.258			5.707	0.008	
	MIN, MAX	3.639, 12.067			2.159, 7.652	0.003, 0.012	
	5%, 95%	3.639, 12.067			2.159, 7.652	0.003, 0.012	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2453	3	2	0.1489
	MEAN, GEO MEAN	5.211, 5.015	0.006, 0.005		5.608, 5.258	0.006, 0.005	
	SD, SE	2.0011, 1.4150	0.0021, 0.0015		2.5268, 1.4588	0.0035, 0.0025	
	MEDIAN	5.211	0.006		4.773	0.006	
	MIN, MAX	3.796, 6.626	0.004, 0.007		3.605, 8.447	0.003, 0.008	
	5%, 95%	3.796, 6.626	0.004, 0.007		3.605, 8.447	0.003, 0.008	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0765	3	3	0.0809
	MEAN, GEO MEAN	7.855, 7.202	0.005, 0.005		4.896, 4.578	0.008, 0.007	
	SD, SE	3.5074, 2.0250	0.0012, 0.0007		2.1454, 1.2386	0.0040, 0.0023	
	MEDIAN	9.241	0.004		4.653	0.008	
	MIN, MAX	3.866, 10.457	0.004, 0.006		2.883, 7.153	0.004, 0.012	
	5%, 95%	3.866, 10.457	0.004, 0.006		2.883, 7.153	0.004, 0.012	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 186 of 264)

Biomarker: Nicotine (µg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1386	3	1	NA
	MEAN, GEO MEAN	1.517, 1.362	0.001, 0.001		0.634, 0.567	0.001, 0.001	
	SD, SE	0.7389, 0.4266	0.0000, 0.0000		0.3133, 0.1809	NA, NA	
	MEDIAN	1.821	0.001		0.754	0.001	
	MIN, MAX	0.675, 2.056	0.001, 0.001		0.278, 0.869	0.001, 0.001	
	5%, 95%	0.675, 2.056	0.001, 0.001		0.278, 0.869	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	1.241, 1.108			0.839, 0.738	0.001, NA	
	SD, SE	0.6858, 0.3959			0.4518, 0.2609	0.0014, 0.0010	
	MEDIAN	1.177			0.926	0.001	
	MIN, MAX	0.590, 1.957			0.350, 1.241	0.000, 0.002	
	5%, 95%	0.590, 1.957			0.350, 1.241	0.000, 0.002	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2207	3	2	0.1489
	MEAN, GEO MEAN	0.846, 0.814	0.001, 0.001		0.910, 0.853	0.001, NA	
	SD, SE	0.3246, 0.2295	0.0000, 0.0000		0.4097, 0.2365	0.0007, 0.0005	
	MEDIAN	0.846	0.001		0.774	0.001	
	MIN, MAX	0.616, 1.075	0.001, 0.001		0.585, 1.370	0.000, 0.001	
	5%, 95%	0.616, 1.075	0.001, 0.001		0.585, 1.370	0.000, 0.001	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0636	3	3	0.0809
	MEAN, GEO MEAN	1.274, 1.168	0.001, 0.001		0.794, 0.742	0.001, NA	
	SD, SE	0.5689, 0.3285	0.0000, 0.0000		0.3481, 0.2010	0.0010, 0.0006	
	MEDIAN	1.499	0.001		0.755	0.001	
	MIN, MAX	0.627, 1.696	0.001, 0.001		0.467, 1.160	0.000, 0.002	
	5%, 95%	0.627, 1.696	0.001, 0.001		0.467, 1.160	0.000, 0.002	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 187 of 264)

Biomarker: Nicotine ((nmol/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.746, 0.710			0.163, 0.153		
	SD, SE	0.2875, 0.1660			0.0685, 0.0396		
	MEDIAN	0.694			0.162		
	MIN, MAX	0.488, 1.056			0.095, 0.232		
	5%, 95%	0.488, 1.056			0.095, 0.232		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.608, 0.525			0.556, 0.340		
	SD, SE	0.4235, 0.2445			0.6289, 0.3631		
	MEDIAN	0.364			0.285		
	MIN, MAX	0.363, 1.097			0.108, 1.275		
	5%, 95%	0.363, 1.097			0.108, 1.275		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.593, 0.591			0.618, 0.406		
	SD, SE	0.0573, 0.0405			0.6858, 0.3959		
	MEDIAN	0.593			0.265		
	MIN, MAX	0.552, 0.633			0.180, 1.408		
	5%, 95%	0.552, 0.633			0.180, 1.408		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.631, 0.601			0.445, 0.325		
	SD, SE	0.2449, 0.1414			0.4370, 0.2523		
	MEDIAN	0.564			0.232		
	MIN, MAX	0.426, 0.902			0.156, 0.948		
	5%, 95%	0.426, 0.902			0.156, 0.948		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 188 of 264)

Biomarker: Nicotine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.121, 0.115			0.026, 0.025		
	SD, SE	0.0465, 0.0269			0.0115, 0.0066		
	MEDIAN	0.113			0.026		
	MIN, MAX	0.079, 0.171			0.015, 0.038		
	5%, 95%	0.079, 0.171			0.015, 0.038		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.099, 0.085			0.090, 0.056		
	SD, SE	0.0687, 0.0397			0.1020, 0.0589		
	MEDIAN	0.059			0.046		
	MIN, MAX	0.059, 0.178			0.018, 0.207		
	5%, 95%	0.059, 0.178			0.018, 0.207		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.097, 0.096			0.100, 0.066		
	SD, SE	0.0092, 0.0065			0.1111, 0.0641		
	MEDIAN	0.097			0.043		
	MIN, MAX	0.090, 0.103			0.029, 0.228		
	5%, 95%	0.090, 0.103			0.029, 0.228		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^a	N	3		NA	3		NA
	MEAN, GEO MEAN	0.102, 0.097			0.072, 0.053		
	SD, SE	0.0395, 0.0228			0.0710, 0.0410		
	MEDIAN	0.092			0.038		
	MIN, MAX	0.069, 0.146			0.025, 0.154		
	5%, 95%	0.069, 0.146			0.025, 0.154		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 189 of 264)

Biomarker: Nicotine (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1386	3	1	NA
	MEAN, GEO MEAN	12271.5, 9840.3	3.4, 3.4		2122.6, 2006.9	3.4, 3.4	
	SD, SE	8510.73, 4913.67	0.00, 0.00		871.69, 503.27	NA, NA	
	MEDIAN	12357.7	3.4		1940.2	3.4	
	MIN, MAX	3718.0, 20738.8	3.4, 3.4		1356.6, 3071.1	3.4, 3.4	
	5%, 95%	3718.0, 20738.8	3.4, 3.4		1356.6, 3071.1	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1386
	MEAN, GEO MEAN	9033.2, 6684.7			3079.6, 2638.5	3.4, 3.4	
	SD, SE	6416.07, 3704.32			2203.98, 1272.47	0.00, 0.00	
	MEDIAN	10778.2			1809.1	3.4	
	MIN, MAX	1925.1, 14396.2			1805.1, 5624.5	3.4, 3.4	
	5%, 95%	1925.1, 14396.2			1805.1, 5624.5	3.4, 3.4	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2207	3	2	0.1386
	MEAN, GEO MEAN	3417.6, 2856.3	3.4, 3.4		3389.0, 3052.9	3.4, 3.4	
	SD, SE	2653.91, 1876.60	0.00, 0.00		1624.09, 937.67	0.00, 0.00	
	MEDIAN	3417.6	3.4		4113.9	3.4	
	MIN, MAX	1541.0, 5294.2	3.4, 3.4		1528.7, 4524.4	3.4, 3.4	
	5%, 95%	1541.0, 5294.2	3.4, 3.4		1528.7, 4524.4	3.4, 3.4	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall*	N	3	3	0.0636	3	3	0.0636
	MEAN, GEO MEAN	9146.4, 7200.5	3.4, 3.4		2863.7, 2640.9	3.4, 3.4	
	SD, SE	5924.46, 3420.49	0.00, 0.00		1355.68, 782.70	0.00, 0.00	
	MEDIAN	11568.0	3.4		2756.6	3.4	
	MIN, MAX	2394.7, 13476.4	3.4, 3.4		1564.8, 4269.8	3.4, 3.4	
	5%, 95%	2394.7, 13476.4	3.4, 3.4		1564.8, 4269.8	3.4, 3.4	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 190 of 264)

Biomarker: Nicotine (ng/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1386	3	1	NA
	MEAN, GEO MEAN	1990.4, 1596.1	0.6, 0.6		344.3, 325.5	0.6, 0.6	
	SD, SE	1380.40, 796.98	0.00, 0.00		141.39, 81.63	NA, NA	
	MEDIAN	2004.4	0.6		314.7	0.6	
	MIN, MAX	603.1, 3363.8	0.6, 0.6		220.0, 498.1	0.6, 0.6	
	5%, 95%	603.1, 3363.8	0.6, 0.6		220.0, 498.1	NA, NA	
	# of BLQ/ALQ Values	0/0	2/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1386
	MEAN, GEO MEAN	1465.2, 1084.3			499.5, 427.9	0.6, 0.6	
	SD, SE	1040.67, 600.83			357.50, 206.40	0.00, 0.00	
	MEDIAN	1748.2			293.4	0.6	
	MIN, MAX	312.3, 2335.1			292.8, 912.3	0.6, 0.6	
	5%, 95%	312.3, 2335.1			292.8, 912.3	0.6, 0.6	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2207	3	2	0.1386
	MEAN, GEO MEAN	554.4, 463.3	0.6, 0.6		549.7, 495.2	0.6, 0.6	
	SD, SE	430.42, 304.35	0.00, 0.00		263.42, 152.09	0.00, 0.00	
	MEDIAN	554.4	0.6		667.3	0.6	
	MIN, MAX	250.0, 858.7	0.6, 0.6		248.0, 733.9	0.6, 0.6	
	5%, 95%	250.0, 858.7	0.6, 0.6		248.0, 733.9	0.6, 0.6	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall*	N	3	3	0.0636	3	3	0.0636
	MEAN, GEO MEAN	1483.6, 1168.0	0.6, 0.6		464.5, 428.3	0.6, 0.6	
	SD, SE	960.91, 554.78	0.00, 0.00		219.92, 126.97	0.00, 0.00	
	MEDIAN	1876.3	0.6		447.1	0.6	
	MIN, MAX	388.5, 2185.9	0.6, 0.6		253.8, 692.6	0.6, 0.6	
	5%, 95%	388.5, 2185.9	0.6, 0.6		253.8, 692.6	0.6, 0.6	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 191 of 264)

Biomarker: Nicotine ((nmol/L)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	961.7, 831.8			89.6, 88.0		
	SD, SE	665.06, 383.97			20.23, 11.68		
	MEDIAN	619.7			93.1		
	MIN, MAX	537.3, 1728.2			67.8, 107.8		
	5%, 95%	537.3, 1728.2			67.8, 107.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	680.0, 514.0			372.7, 197.1		
	SD, SE	571.33, 329.86			489.02, 282.33		
	MEDIAN	538.9			90.5		
	MIN, MAX	192.5, 1308.7			90.3, 937.4		
	5%, 95%	192.5, 1308.7			90.3, 937.4		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	349.0, 336.6			337.8, 236.2		
	SD, SE	130.39, 92.20			313.71, 181.12		
	MEDIAN	349.0			251.4		
	MIN, MAX	256.8, 441.2			76.4, 685.7		
	5%, 95%	256.8, 441.2			76.4, 685.7		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	684.6, 605.8			266.7, 188.5		
	SD, SE	421.12, 243.13			266.90, 154.09		
	MEDIAN	538.1			149.8		
	MIN, MAX	356.3, 1159.4			78.2, 572.1		
	5%, 95%	356.3, 1159.4			78.2, 572.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 192 of 264)

Biomarker: Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	156.0, 134.9			14.5, 14.3		
	SD, SE	107.88, 62.29			3.29, 1.90		
	MEDIAN	100.5			15.1		
	MIN, MAX	87.1, 280.3			11.0, 17.5		
	5%, 95%	87.1, 280.3			11.0, 17.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	110.3, 83.3			60.5, 32.0		
	SD, SE	92.70, 53.52			79.36, 45.82		
	MEDIAN	87.4			14.7		
	MIN, MAX	31.2, 212.3			14.6, 152.1		
	5%, 95%	31.2, 212.3			14.6, 152.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	56.7, 54.6			54.8, 38.3		
	SD, SE	21.14, 14.95			50.87, 29.37		
	MEDIAN	56.7			40.8		
	MIN, MAX	41.7, 71.6			12.4, 111.2		
	5%, 95%	41.7, 71.6			12.4, 111.2		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	111.1, 98.3			43.3, 30.6		
	SD, SE	68.32, 39.45			43.29, 24.99		
	MEDIAN	87.3			24.3		
	MIN, MAX	57.8, 188.1			12.7, 92.8		
	5%, 95%	57.8, 188.1			12.7, 92.8		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439360

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 193 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	3609.8, 1906.8	9.3, 9.3		1593.8, 1512.8	9.3, 9.3	
	SD, SE	4207.14, 2428.99	NA, NA		653.29, 377.18	NA, NA	
	MEDIAN	2052.5	9.3		1331.9	9.3	
	MIN, MAX	403.4, 8373.6	9.3, 9.3		1112.1, 2337.4	9.3, 9.3	
	5%, 95%	403.4, 8373.6	NA, NA		1112.1, 2337.4	NA, NA	
	# of BLQ/ALQ Values	0/0	1/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	4013.5, 3366.0			1742.3, 1662.4	27.7, 20.7	
	SD, SE	2738.64, 1581.16			648.77, 374.57	25.95, 18.35	
	MEDIAN	3518.6			1648.3	27.7	
	MIN, MAX	1556.0, 6965.8			1145.6, 2432.9	9.3, 46.0	
	5%, 95%	1556.0, 6965.8			1145.6, 2432.9	9.3, 46.0	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2207	3	2	0.1386
	MEAN, GEO MEAN	2136.0, 1288.9	9.3, 9.3		1660.5, 1587.1	9.3, 9.3	
	SD, SE	2408.76, 1703.25	0.00, 0.00		640.98, 370.07	0.00, 0.00	
	MEDIAN	2136.0	9.3		1299.6	9.3	
	MIN, MAX	432.7, 3839.2	9.3, 9.3		1281.4, 2400.6	9.3, 9.3	
	5%, 95%	432.7, 3839.2	9.3, 9.3		1281.4, 2400.6	9.3, 9.3	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0636	3	3	0.0765
	MEAN, GEO MEAN	3325.3, 2421.6	9.3, 9.3		1665.5, 1590.4	13.4, 12.3	
	SD, SE	2836.52, 1637.67	0.00, 0.00		639.69, 369.33	7.04, 4.07	
	MEDIAN	2785.6	9.3		1426.6	9.3	
	MIN, MAX	797.4, 6392.9	9.3, 9.3		1179.7, 2390.3	9.3, 21.5	
	5%, 95%	797.4, 6392.9	9.3, 9.3		1179.7, 2390.3	9.3, 21.5	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 194 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	284.7, 161.1			66.8, 66.3		
	SD, SE	357.90, 206.63			9.83, 5.68		
	MEDIAN	89.2			70.8		
	MIN, MAX	67.2, 697.8			55.6, 74.0		
	5%, 95%	67.2, 697.8			55.6, 74.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	321.6, 258.8			181.7, 124.2		
	SD, SE	270.13, 155.96			194.19, 112.12		
	MEDIAN	175.9			82.4		
	MIN, MAX	155.6, 633.3			57.3, 405.5		
	5%, 95%	155.6, 633.3			57.3, 405.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	196.0, 151.9			178.8, 122.8		
	SD, SE	175.22, 123.90			191.69, 110.67		
	MEDIAN	196.0			72.2		
	MIN, MAX	72.1, 319.9			64.1, 400.1		
	5%, 95%	72.1, 319.9			64.1, 400.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	260.4, 192.9			142.4, 109.5		
	SD, SE	251.65, 145.29			129.90, 75.00		
	MEDIAN	132.6			76.2		
	MIN, MAX	98.3, 550.3			59.0, 292.1		
	5%, 95%	98.3, 550.3			59.0, 292.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 195 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/24hr) Analytical Lab: INBIFO		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	3712.727, 2363.769	27.900, 27.900		3729.771, 3457.328	11.160, 11.160	
	SD, SE	3386.7049, 1955.3150	NA, NA		1798.4364, 1038.3277	NA, NA	
	MEDIAN	3304.525	27.900		3225.090	11.160	
	MIN, MAX	548.624, 7285.032	27.900, 27.900		2237.592, 5726.630	11.160, 11.160	
	5%, 95%	548.624, 7285.032	NA, NA		2237.592, 5726.630	NA, NA	
	# of BLQ/ALQ Values	0/0	1/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	4306.237, 4043.739			4015.243, 3928.435	39.730, 38.893	
	SD, SE	1923.8454, 1110.7327			1062.4322, 613.3955	11.4693, 8.1100	
	MEDIAN	3624.158			3551.360	39.730	
	MIN, MAX	2816.360, 6478.194			3263.634, 5230.735	31.620, 47.840	
	5%, 95%	2816.360, 6478.194			3263.634, 5230.735	31.620, 47.840	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2453	3	2	0.1489
	MEAN, GEO MEAN	3273.943, 1885.034	17.968, 17.926		3447.031, 3209.515	20.739, 18.674	
	SD, SE	3785.5909, 2676.8170	1.7359, 1.2275		1583.0338, 913.9650	12.7576, 9.0210	
	MEDIAN	3273.943	17.968		3139.430	20.739	
	MIN, MAX	597.126, 5950.760	16.740, 19.195		2040.372, 5161.290	11.718, 29.760	
	5%, 95%	597.126, 5950.760	16.740, 19.195		2040.372, 5161.290	11.718, 29.760	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	3785.458, 3109.518	21.278, 20.774		3730.681, 3547.479	28.318, 28.098	
	SD, SE	2640.0009, 1524.2053	5.8644, 3.3858		1476.2161, 852.2937	4.2129, 2.4323	
	MEDIAN	3464.342	19.195		3305.293	29.760	
	MIN, MAX	1320.703, 6571.329	16.740, 27.900		2513.866, 5372.885	23.573, 31.620	
	5%, 95%	1320.703, 6571.329	16.740, 27.900		2513.866, 5372.885	23.573, 31.620	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234) will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 196 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	280.733, 199.795			133.033, 151.520		
	SD, SE	283.8346, 163.8720			25.6207, 14.7921		
	MEDIAN	143.675			161.255		
	MIN, MAX	91.437, 607.086			124.311, 173.534		
	5%, 95%	91.437, 607.086			124.311, 173.534		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	350.590, 310.915			404.180, 293.415		
	SD, SE	212.4258, 122.6441			405.0254, 233.8415		
	MEDIAN	281.636			177.568		
	MIN, MAX	181.208, 588.927			163.182, 871.789		
	5%, 95%	181.208, 588.927			163.182, 871.789		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	297.709, 222.153			376.847, 248.288		
	SD, SE	280.2802, 198.1880			419.1767, 242.0118		
	MEDIAN	297.709			156.972		
	MIN, MAX	99.521, 495.897			113.354, 860.215		
	5%, 95%	99.521, 495.897			113.354, 860.215		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	294.648, 243.467			311.353, 241.164		
	SD, SE	233.2529, 134.6686			280.8874, 162.1704		
	MEDIAN	162.442			165.265		
	MIN, MAX	157.531, 563.970			133.616, 635.179		
	5%, 95%	157.531, 563.970			133.616, 635.179		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 197 of 264)

Biomarker: Nicotine-N-glucuronide (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	2.478, 1.628	0.011, 0.011		3.022, 2.636	0.014, 0.014	
	SD, SE	2.3928, 1.3815	NA, NA		1.6021, 0.9250	NA, NA	
	MEDIAN	1.864	0.011		3.809	0.014	
	MIN, MAX	0.452, 5.118	0.011, 0.011		1.179, 4.079	0.014, 0.014	
	5%, 95%	0.452, 5.118	NA, NA		1.179, 4.079	NA, NA	
	# of BLQ/ALQ Values	0/0	1/0		0/0	1/0	
Week 2	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	3.716, 3.439			2.965, 2.868	0.036, 0.036	
	SD, SE	1.8604, 1.0741			0.8736, 0.5044	0.0042, 0.0030	
	MEDIAN	2.941			3.310	0.036	
	MIN, MAX	2.369, 5.839			1.972, 3.614	0.033, 0.039	
	5%, 95%	2.369, 5.839			1.972, 3.614	0.033, 0.039	
	# of BLQ/ALQ Values	0/0			0/0	2/0	
Week 3	N	2	2	0.2453	3	2	0.1489
	MEAN, GEO MEAN	2.936, 2.263	0.015, 0.014		3.107, 2.733	0.015, 0.014	
	SD, SE	2.6439, 1.8695	0.0057, 0.0040		1.7805, 1.0280	0.0085, 0.0060	
	MEDIAN	2.936	0.015		3.022	0.015	
	MIN, MAX	1.066, 4.805	0.011, 0.019		1.371, 4.929	0.009, 0.021	
	5%, 95%	1.066, 4.805	0.011, 0.019		1.371, 4.929	0.009, 0.021	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Overall ^b	N	3	3	0.0765	3	3	0.0809
	MEAN, GEO MEAN	2.952, 2.547	0.014, 0.013		3.032, 2.783	0.025, 0.024	
	SD, SE	2.0181, 1.1652	0.0046, 0.0027		1.3568, 0.7833	0.0069, 0.0040	
	MEDIAN	2.117	0.011		3.482	0.021	
	MIN, MAX	1.486, 5.254	0.011, 0.019		1.507, 4.106	0.021, 0.033	
	5%, 95%	1.486, 5.254	0.011, 0.019		1.507, 4.106	0.021, 0.033	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 198 of 264)

Biomarker: Nicotine-N-glucuronide ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male			Female	
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	0.194, 0.137			0.127, 0.116	
	SD, SE	0.2015, 0.1163			0.0620, 0.0358	
	MEDIAN	0.081			0.124	
	MIN, MAX	0.075, 0.427			0.066, 0.190	
	5%, 95%	0.075, 0.427			0.066, 0.190	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	0.314, 0.264			0.277, 0.215	
	SD, SE	0.2072, 0.1197			0.2414, 0.1394	
	MEDIAN	0.294			0.181	
	MIN, MAX	0.118, 0.531			0.099, 0.552	
	5%, 95%	0.118, 0.531			0.099, 0.552	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	0.289, 0.267			0.350, 0.211	
	SD, SE	0.1570, 0.1110			0.4108, 0.2372	
	MEDIAN	0.289			0.151	
	MIN, MAX	0.178, 0.400			0.076, 0.822	
	5%, 95%	0.178, 0.400			0.076, 0.822	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	0.245, 0.202			0.251, 0.191	
	SD, SE	0.1847, 0.1067			0.2199, 0.1269	
	MEDIAN	0.182			0.174	
	MIN, MAX	0.100, 0.453			0.080, 0.499	
	5%, 95%	0.100, 0.453			0.080, 0.499	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 199 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/mg Creatinine) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	41.322, 36.551			62.078, 54.495	0.084, 0.078	
	SD, SE	21.2363, 12.2608			37.5785, 21.6960	0.0403, 0.0285	
	MEDIAN	49.312			54.500	0.084	
	MIN, MAX	17.250, 57.405			28.866, 102.868	0.055, 0.112	
	5%, 95%	17.250, 57.405			28.866, 102.868	0.055, 0.112	
	# of BLQ/ALQ Values	0/0			0/0	0/0	
Week 2	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	46.686, 44.322	0.075, 0.075		65.290, 55.483	0.069, 0.069	
	SD, SE	17.1325, 9.8915	NA, NA		45.4552, 26.2436	0.0099, 0.0070	
	MEDIAN	50.181	0.075		50.462	0.069	
	MIN, MAX	28.075, 61.801	0.075, 0.075		29.101, 116.308	0.062, 0.076	
	5%, 95%	28.075, 61.801	NA, NA		29.101, 116.308	0.062, 0.076	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	3	0.1489	3	1	NA
	MEAN, GEO MEAN	37.976, 33.319	0.062, 0.061		56.497, 49.055	0.036, 0.036	
	SD, SE	25.7698, 18.2220	0.0172, 0.0099		34.1962, 19.7432	NA, NA	
	MEDIAN	37.976	0.068		53.238	0.036	
	MIN, MAX	19.754, 56.198	0.043, 0.076		24.047, 92.206	0.036, 0.036	
	5%, 95%	19.754, 56.198	0.043, 0.076		24.047, 92.206	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^a	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	43.303, 39.811	0.064, 0.062		61.288, 53.089	0.073, 0.069	
	SD, SE	19.2158, 11.0943	0.0180, 0.0104		38.9394, 22.4817	0.0304, 0.0215	
	MEDIAN	49.747	0.072		52.733	0.073	
	MIN, MAX	21.693, 58.468	0.043, 0.076		27.338, 103.794	0.051, 0.094	
	5%, 95%	21.693, 58.468	0.043, 0.076		27.338, 103.794	0.051, 0.094	

^a P-value from Wilcoxon rank-sum test.^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439367

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 200 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	3.268, 3.089			2.800, 2.389		
	SD, SE	1.3631, 0.7870			2.0295, 1.1717		
	MEDIAN	2.875			1.652		
	MIN, MAX	2.144, 4.784			1.604, 5.143		
	5%, 95%	2.144, 4.784			1.604, 5.143		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	3.645, 3.408			5.227, 4.144		
	SD, SE	1.7152, 0.9903			3.5146, 2.0292		
	MEDIAN	2.808			5.815		
	MIN, MAX	2.509, 5.618			1.455, 8.410		
	5%, 95%	2.509, 5.618			1.455, 8.410		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	3.988, 3.926			4.940, 3.795		
	SD, SE	0.9836, 0.6955			3.7793, 2.1820		
	MEDIAN	3.988			4.610		
	MIN, MAX	3.292, 4.683			1.336, 8.873		
	5%, 95%	3.292, 4.683			1.336, 8.873		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	3.449, 3.271			4.322, 3.634		
	SD, SE	1.4073, 0.8125			2.5371, 1.4648		
	MEDIAN	2.992			5.189		
	MIN, MAX	2.327, 5.028			1.465, 6.312		
	5%, 95%	2.327, 5.028			1.465, 6.312		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 201 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/mg Creatinine) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3	2	0.1386
	MEAN, GEO MEAN	0.007, 0.006			0.010, 0.009	0.000, NA	
	SD, SE	0.0032, 0.0019			0.0061, 0.0035	0.0000, 0.0000	
	MEDIAN	0.008			0.009	0.000	
	MIN, MAX	0.003, 0.009			0.005, 0.017	0.000, 0.000	
	5%, 95%	0.003, 0.009			0.005, 0.017	0.000, 0.000	
	# of BLQ/ALQ Values	0/0			0/0	0/0	
Week 2	N	3	1	NA	3	2	0.1386
	MEAN, GEO MEAN	0.008, 0.007	0.000, NA		0.011, 0.009	0.000, NA	
	SD, SE	0.0025, 0.0015	NA, NA		0.0074, 0.0043	0.0000, 0.0000	
	MEDIAN	0.008	0.000		0.008	0.000	
	MIN, MAX	0.005, 0.010	0.000, 0.000		0.005, 0.019	0.000, 0.000	
	5%, 95%	0.005, 0.010	NA, NA		0.005, 0.019	0.000, 0.000	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	3	0.1066	3	1	NA
	MEAN, GEO MEAN	0.006, 0.005	0.000, NA		0.009, 0.008	0.000, NA	
	SD, SE	0.0042, 0.0030	0.0000, 0.0000		0.0055, 0.0032	NA, NA	
	MEDIAN	0.006	0.000		0.009	0.000	
	MIN, MAX	0.003, 0.009	0.000, 0.000		0.004, 0.015	0.000, 0.000	
	5%, 95%	0.003, 0.009	0.000, 0.000		0.004, 0.015	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	3	0.0636	3	2	0.1386
	MEAN, GEO MEAN	0.007, 0.007	0.000, NA		0.010, 0.009	0.000, NA	
	SD, SE	0.0026, 0.0015	0.0000, 0.0000		0.0061, 0.0035	0.0000, 0.0000	
	MEDIAN	0.008	0.000		0.009	0.000	
	MIN, MAX	0.004, 0.009	0.000, 0.000		0.005, 0.017	0.000, 0.000	
	5%, 95%	0.004, 0.009	0.000, 0.000		0.005, 0.017	0.000, 0.000	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 202 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.000, NA			0.000, NA		
	SD, SE	0.0006, 0.0003			0.0006, 0.0003		
	MEDIAN	0.000			0.000		
	MIN, MAX	0.000, 0.001			0.000, 0.001		
	5%, 95%	0.000, 0.001			0.000, 0.001		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.000, NA			0.001, NA		
	SD, SE	0.0006, 0.0003			0.0006, 0.0003		
	MEDIAN	0.000			0.001		
	MIN, MAX	0.000, 0.001			0.000, 0.001		
	5%, 95%	0.000, 0.001			0.000, 0.001		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.001, 0.001			0.001, NA		
	SD, SE	0.0000, 0.0000			0.0006, 0.0003		
	MEDIAN	0.001			0.001		
	MIN, MAX	0.001, 0.001			0.000, 0.001		
	5%, 95%	0.001, 0.001			0.000, 0.001		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	0.000, NA			0.001, NA		
	SD, SE	0.0006, 0.0003			0.0006, 0.0003		
	MEDIAN	0.000			0.001		
	MIN, MAX	0.000, 0.001			0.000, 0.001		
	5%, 95%	0.000, 0.001			0.000, 0.001		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 203 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3	2	0.1489
	MEAN, GEO MEAN	63355.867, 53088.630			72805.883, 71479.861	79.565, 70.830	
	SD, SE	36835.3562, 21266.9028			16470.6257, 9509.3202	51.2575, 36.2445	
	MEDIAN	81705.702			76509.580	79.565	
	MIN, MAX	20949.848, 87412.052			54798.744, 87109.330	43.320, 115.809	
	5%, 95%	20949.848, 87412.052			54798.744, 87109.330	43.320, 115.809	
	# of BLQ/ALQ Values	0/0			0/0	0/0	
Week 2	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	57401.474, 52106.544	104.690, 104.690		80736.256, 76003.456	89.750, 88.645	
	SD, SE	26746.5027, 15442.1006	NA, NA		33073.8893, 19095.2189	19.8527, 14.0380	
	MEDIAN	68568.714	104.690		79743.285	89.750	
	MIN, MAX	26881.034, 76754.673	104.690, 104.690		48170.034, 114295.450	75.712, 103.788	
	5%, 95%	26881.034, 76754.673	NA, NA		48170.034, 114295.450	75.712, 103.788	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	3	0.1489	3	1	NA
	MEAN, GEO MEAN	40332.687, 27754.070	81.394, 79.732		62439.570, 57600.129	45.486, 45.486	
	SD, SE	41386.8871, 29264.9485	20.7304, 11.9687		30551.0653, 17638.6658	NA, NA	
	MEDIAN	40332.687	74.511		55742.835	45.486	
	MIN, MAX	11067.738, 69597.635	64.980, 104.690		35792.389, 95783.485	45.486, 45.486	
	5%, 95%	11067.738, 69597.635	64.980, 104.690		35792.389, 95783.485	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	58335.640, 49063.959	81.394, 79.732		71993.903, 68667.984	82.319, 77.597	
	SD, SE	33804.6732, 19517.1372	20.7304, 11.9687		26429.5765, 15259.1231	38.8626, 27.4800	
	MEDIAN	73290.684	74.511		70665.233	82.319	
	MIN, MAX	19632.873, 82083.363	64.980, 104.690		46253.722, 99062.755	54.839, 109.799	
	5%, 95%	19632.873, 82083.363	64.980, 104.690		46253.722, 99062.755	54.839, 109.799	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 204 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((nmol/24hr/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	4700.325, 4487.262			3239.438, 3132.648		
	SD, SE	1832.5206, 1058.0063			1032.4119, 596.0633		
	MEDIAN	3800.524			3044.375		
	MIN, MAX	3491.641, 6808.809			2318.472, 4355.467		
	5%, 95%	3491.641, 6808.809			2318.472, 4355.467		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	4253.119, 4006.373			7137.941, 5676.705		
	SD, SE	1808.8400, 1044.3342			5578.8697, 3220.9619		
	MEDIAN	3837.734			5714.773		
	MIN, MAX	2688.103, 6233.519			2408.502, 13290.548		
	5%, 95%	2688.103, 6233.519			2408.502, 13290.548		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	3822.213, 3270.849			5356.038, 4455.935		
	SD, SE	2796.7346, 1977.5900			3683.8604, 2126.8778		
	MEDIAN	3822.213			4789.174		
	MIN, MAX	1844.623, 5799.803			1988.466, 9290.473		
	5%, 95%	1844.623, 5799.803			1988.466, 9290.473		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	4258.209, 4003.325			5244.472, 4671.897		
	SD, SE	1842.6232, 1063.8390			2920.6098, 1686.2148		
	MEDIAN	3819.129			4953.138		
	MIN, MAX	2674.789, 6280.710			2480.448, 8299.831		
	5%, 95%	2674.789, 6280.710			2480.448, 8299.831		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as 1.234) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 205 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/24hr)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male			Female	
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers
Week 1	N	3		NA	3	2
	MEAN, GEO MEAN	10.278, 8.613			11.811, 11.596	0.013, 0.012
	SD, SE	5.9756, 3.4500			2.6721, 1.5428	0.0085, 0.0060
	MEDIAN	13.255			12.412	0.013
	MIN, MAX	3.399, 14.181			8.890, 14.132	0.007, 0.019
	5%, 95%	3.399, 14.181			8.890, 14.132	0.007, 0.019
	# of BLQ/ALQ Values	0/0			0/0	0/0
Week 2	N	3	1	NA	3	2
	MEAN, GEO MEAN	9.312, 8.453	0.017, 0.017		13.098, 12.330	0.015, 0.014
	SD, SE	4.3391, 2.5052	NA, NA		5.3653, 3.0977	0.0035, 0.0025
	MEDIAN	11.124	0.017		12.937	0.015
	MIN, MAX	4.361, 12.452	0.017, 0.017		7.815, 18.542	0.012, 0.017
	5%, 95%	4.361, 12.452	NA, NA		7.815, 18.542	0.012, 0.017
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0
Week 3	N	2	3	0.1489	3	1
	MEAN, GEO MEAN	6.544, 4.503	0.013, 0.013		10.130, 9.345	0.007, 0.007
	SD, SE	6.7140, 4.7475	0.0032, 0.0019		4.9562, 2.8614	NA, NA
	MEDIAN	6.544	0.012		9.043	0.007
	MIN, MAX	1.796, 11.291	0.011, 0.017		5.807, 15.539	0.007, 0.007
	5%, 95%	1.796, 11.291	0.011, 0.017		5.807, 15.539	NA, NA
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0
Overall ^b	N	3	3	0.0809	3	2
	MEAN, GEO MEAN	9.464, 7.960	0.013, 0.013		11.680, 11.140	0.014, 0.013
	SD, SE	5.4844, 3.1664	0.0032, 0.0019		4.2876, 2.4754	0.0064, 0.0045
	MEDIAN	11.890	0.012		11.464	0.014
	MIN, MAX	3.185, 13.317	0.011, 0.017		7.504, 16.071	0.009, 0.018
	5%, 95%	3.185, 13.317	0.011, 0.017		7.504, 16.071	0.009, 0.018

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 206 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites ((mg/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.763, 0.728			0.526, 0.508		
	SD, SE	0.2976, 0.1718			0.1678, 0.0969		
	MEDIAN	0.617			0.494		
	MIN, MAX	0.566, 1.105			0.376, 0.707		
	5%, 95%	0.566, 1.105			0.376, 0.707		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.690, 0.650			1.158, 0.921		
	SD, SE	0.2933, 0.1693			0.9049, 0.5224		
	MEDIAN	0.623			0.927		
	MIN, MAX	0.436, 1.011			0.391, 2.156		
	5%, 95%	0.436, 1.011			0.391, 2.156		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.620, 0.530			0.869, 0.723		
	SD, SE	0.4540, 0.3210			0.5973, 0.3449		
	MEDIAN	0.620			0.777		
	MIN, MAX	0.299, 0.941			0.323, 1.507		
	5%, 95%	0.299, 0.941			0.323, 1.507		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.691, 0.650			0.851, 0.758		
	SD, SE	0.2989, 0.1726			0.4733, 0.2732		
	MEDIAN	0.620			0.804		
	MIN, MAX	0.434, 1.019			0.403, 1.346		
	5%, 95%	0.434, 1.019			0.403, 1.346		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 207 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3	2	0.1386
	MEAN, GEO MEAN	54537.4, 42825.9			31294.8, 31277.1	36.1, 36.1	
	SD, SE	39255.72, 22664.30			1291.58, 745.69	0.00, 0.00	
	MEDIAN	54293.2			31228.4	36.1	
	MIN, MAX	15404.3, 93914.6			30037.7, 32618.3	36.1, 36.1	
	5%, 95%	15404.3, 93914.6			30037.7, 32618.3	36.1, 36.1	
	# of BLQ/ALQ Values	0/0			0/0	0/0	
Week 2	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	54366.8, 43373.7	36.1, 36.1		32762.6, 32162.1	54.5, 51.3	
	SD, SE	34223.59, 19759.00	NA, NA		7305.12, 4217.61	25.95, 18.35	
	MEDIAN	73729.8	36.1		36869.5	54.5	
	MIN, MAX	14851.4, 74519.1	36.1, 36.1		24328.3, 37089.9	36.1, 72.8	
	5%, 95%	14851.4, 74519.1	NA, NA		24328.3, 37089.9	36.1, 72.8	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	3	0.1066	3	1	NA
	MEAN, GEO MEAN	26460.9, 18976.7	36.1, 36.1		29273.3, 28483.2	36.1, 36.1	
	SD, SE	26079.23, 18440.80	0.00, 0.00		8648.80, 4993.39	NA, NA	
	MEDIAN	26460.9	36.1		25926.9	36.1	
	MIN, MAX	8020.1, 44901.7	36.1, 36.1		22797.7, 39095.3	36.1, 36.1	
	5%, 95%	8020.1, 44901.7	36.1, 36.1		22797.7, 39095.3	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	3	0.0636	3	2	0.1489
	MEAN, GEO MEAN	49337.8, 38757.4	36.1, 36.1		31110.2, 30900.9	42.2, 41.8	
	SD, SE	31841.90, 18383.93	0.00, 0.00		4384.36, 2531.31	8.63, 6.10	
	MEDIAN	64406.2	36.1		31415.1	42.2	
	MIN, MAX	12758.6, 70848.7	36.1, 36.1		26581.4, 35334.2	36.1, 48.3	
	5%, 95%	12758.6, 70848.7	36.1, 36.1		26581.4, 35334.2	36.1, 48.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234" will be used as "1.234") for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 208 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (nmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	4251.4, 3619.8			1420.1, 1370.7		
	SD, SE	3097.59, 1788.40			438.66, 253.26		
	MEDIAN	2567.4			1501.9		
	MIN, MAX	2360.6, 7826.2			946.3, 1812.1		
	5%, 95%	2360.6, 7826.2			946.3, 1812.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	3971.3, 3334.9			3080.5, 2402.2		
	SD, SE	2617.43, 1511.18			2703.93, 1561.11		
	MEDIAN	3726.0			1843.5		
	MIN, MAX	1485.1, 6702.7			1216.4, 6181.7		
	5%, 95%	1485.1, 6702.7			1216.4, 6181.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	2539.3, 2236.4			2514.2, 2203.5		
	SD, SE	1700.66, 1202.55			1602.33, 925.11		
	MEDIAN	2539.3			1954.8		
	MIN, MAX	1336.7, 3741.8			1266.5, 4321.2		
	5%, 95%	1336.7, 3741.8			1266.5, 4321.2		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	3643.3, 3217.1			2338.3, 2129.2		
	SD, SE	2208.89, 1275.30			1291.01, 745.37		
	MEDIAN	3043.3			1766.7		
	MIN, MAX	1796.4, 6090.2			1431.7, 3816.4		
	5%, 95%	1796.4, 6090.2			1431.7, 3816.4		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 209 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/L) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3	2	0.1386
	MEAN, GEO MEAN	8.8, 6.9			5.1, 5.1	0.0, NA	
	SD, SE	6.35, 3.67			0.20, 0.12	0.00, 0.00	
	MEDIAN	8.8			5.1	0.0	
	MIN, MAX	2.5, 15.2			4.9, 5.3	0.0, 0.0	
	5%, 95%	2.5, 15.2			4.9, 5.3	0.0, 0.0	
	# of BLQ/ALQ Values	0/0			0/0	0/0	
Week 2	N	3	1	NA	3	2	0.1281
	MEAN, GEO MEAN	8.8, 7.0	0.0, NA		5.3, 5.2	0.0, NA	
	SD, SE	5.57, 3.22	NA, NA		1.21, 0.70	0.00, 0.00	
	MEDIAN	12.0	0.0		6.0	0.0	
	MIN, MAX	2.4, 12.1	0.0, 0.0		3.9, 6.0	0.0, 0.0	
	5%, 95%	2.4, 12.1	NA, NA		3.9, 6.0	0.0, 0.0	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	3	0.1066	3	1	NA
	MEAN, GEO MEAN	4.3, 3.1	0.0, NA		4.7, 4.6	0.0, NA	
	SD, SE	4.24, 3.00	0.00, 0.00		1.38, 0.80	NA, NA	
	MEDIAN	4.3	0.0		4.2	0.0	
	MIN, MAX	1.3, 7.3	0.0, 0.0		3.7, 6.3	0.0, 0.0	
	5%, 95%	1.3, 7.3	0.0, 0.0		3.7, 6.3	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	3	0.0636	3	2	0.1386
	MEAN, GEO MEAN	8.0, 6.3	0.0, NA		5.0, 5.0	0.0, NA	
	SD, SE	5.16, 2.98	0.00, 0.00		0.70, 0.41	0.00, 0.00	
	MEDIAN	10.5	0.0		5.1	0.0	
	MIN, MAX	2.1, 11.5	0.0, 0.0		4.3, 5.7	0.0, 0.0	
	5%, 95%	2.1, 11.5	0.0, 0.0		4.3, 5.7	0.0, 0.0	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 210 of 264)

Biomarker: Sum of Nicotine and Nicotine metabolites (mg/L/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.7, 0.6			0.2, 0.2		
	SD, SE	0.52, 0.30			0.06, 0.03		
	MEDIAN	0.4			0.2		
	MIN, MAX	0.4, 1.3			0.2, 0.3		
	5%, 95%	0.4, 1.3			0.2, 0.3		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.6, 0.5			0.5, 0.4		
	SD, SE	0.45, 0.26			0.44, 0.25		
	MEDIAN	0.6			0.3		
	MIN, MAX	0.2, 1.1			0.2, 1.0		
	5%, 95%	0.2, 1.1			0.2, 1.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.4, 0.3			0.4, 0.3		
	SD, SE	0.28, 0.20			0.26, 0.15		
	MEDIAN	0.4			0.3		
	MIN, MAX	0.2, 0.6			0.2, 0.7		
	5%, 95%	0.2, 0.6			0.2, 0.7		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.6, 0.5			0.4, 0.3		
	SD, SE	0.36, 0.21			0.21, 0.12		
	MEDIAN	0.5			0.3		
	MIN, MAX	0.3, 1.0			0.2, 0.6		
	5%, 95%	0.3, 1.0			0.2, 0.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 211 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	24791.559, 21723.343	42.241, 38.693		41612.428, 39914.894	62.528, 42.850	
	SD, SE	15099.2521, 8717.5573	23.9631, 16.9445		15356.2861, 8865.9559	62.2237, 35.9249	
	MEDIAN	21746.172	42.241		34072.584	39.779	
	MIN, MAX	11447.120, 41181.385	25.296, 59.185		31483.480, 59281.220	14.880, 132.925	
	5%, 95%	11447.120, 41181.385	25.296, 59.185		31483.480, 59281.220	14.880, 132.925	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	24166.924, 21982.634	42.395, 37.499		45347.306, 39977.300	24.273, 21.442	
	SD, SE	13076.3238, 7549.6191	25.3989, 14.6640		28769.7893, 16610.2456	16.0895, 11.3770	
	MEDIAN	19995.744	35.960		33423.900	24.273	
	MIN, MAX	13685.048, 38819.979	20.832, 70.392		24456.168, 78161.850	12.896, 35.650	
	5%, 95%	13685.048, 38819.979	20.832, 70.392		24456.168, 78161.850	12.896, 35.650	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1489	3	2	0.1489
	MEAN, GEO MEAN	14960.904, 11909.748	27.958, 27.387		33115.950, 25344.502	27.652, 24.899	
	SD, SE	12805.1968, 9054.6415	7.1207, 4.1111		30639.4576, 17689.6991	17.0102, 12.0280	
	MEDIAN	14960.904	25.594		16042.225	27.652	
	MIN, MAX	5906.262, 24015.545	22.320, 35.960		14817.346, 68488.280	15.624, 39.680	
	5%, 95%	5906.262, 24015.545	22.320, 35.960		14817.346, 68488.280	15.624, 39.680	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall*	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	24088.660, 20855.626	36.833, 34.881		40025.228, 35643.758	61.921, 41.943	
	SD, SE	14945.8351, 8628.9819	14.4738, 8.3564		24816.7724, 14327.9702	62.6422, 36.1665	
	MEDIAN	21919.154	35.960		26983.202	38.370	
	MIN, MAX	10346.143, 40000.682	22.816, 51.724		24448.699, 68643.783	14.467, 132.925	
	5%, 95%	10346.143, 40000.682	22.816, 51.724		24448.699, 68643.783	14.467, 132.925	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 212 of 264)

Biomarker: Total 3-hydroxycotinine (µg/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	4764.937, 4175.226	8.119, 7.437		7997.909, 7671.643	12.018, 8.236	
	SD, SE	2902.0764, 1675.5146	4.6054, 3.2565		2951.4778, 1704.0365	11.9592, 6.9046	
	MEDIAN	4179.614	8.119		6548.751	7.646	
	MIN, MAX	2200.136, 7915.062	4.862, 11.375		6051.125, 11393.850	2.860, 25.548	
	5%, 95%	2200.136, 7915.062	4.862, 11.375		6051.125, 11393.850	2.860, 25.548	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0809	3	2	0.1489
	MEAN, GEO MEAN	4644.883, 4225.062	8.148, 7.208		8715.752, 7683.637	4.666, 4.121	
	SD, SE	2513.2695, 1451.0368	4.8814, 2.8183		5529.5538, 3192.4894	3.0922, 2.1865	
	MEDIAN	3843.182	6.912		6424.074	4.666	
	MIN, MAX	2630.266, 7461.200	4.004, 13.529		4700.475, 15022.708	2.479, 6.852	
	5%, 95%	2630.266, 7461.200	4.004, 13.529		4700.475, 15022.708	2.479, 6.852	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1489	3	2	0.1489
	MEAN, GEO MEAN	2875.486, 2289.054	5.374, 5.264		6364.886, 4871.213	5.315, 4.785	
	SD, SE	2461.1587, 1740.3020	1.3689, 0.7903		5888.9034, 3399.9600	3.2690, 2.3115	
	MEDIAN	2875.486	4.919		3083.316	5.315	
	MIN, MAX	1135.184, 4615.788	4.290, 6.912		2847.894, 13163.447	3.003, 7.626	
	5%, 95%	1135.184, 4615.788	4.290, 6.912		2847.894, 13163.447	3.003, 7.626	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall*	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	4629.840, 4008.451	7.079, 6.704		7692.849, 6850.730	11.901, 8.062	
	SD, SE	2872.5893, 1658.4902	2.7818, 1.6061		4769.7834, 2753.8358	12.0395, 6.9510	
	MEDIAN	4212.861	6.912		5186.172	7.375	
	MIN, MAX	1988.529, 7688.131	4.385, 9.941		4699.040, 13193.335	2.781, 25.548	
	5%, 95%	1988.529, 7688.131	4.385, 9.941		4699.040, 13193.335	2.781, 25.548	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 213 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1836.843, 1836.143			1937.009, 1749.204		
	SD, SE	62.4451, 36.0527			1005.7330, 580.6602		
	MEDIAN	1812.181			1892.921		
	MIN, MAX	1790.495, 1907.853			954.045, 2964.061		
	5%, 95%	1790.495, 1907.853			954.045, 2964.061		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1709.100, 1690.203			3567.184, 2985.907		
	SD, SE	301.3276, 173.9716			2193.8771, 1266.6356		
	MEDIAN	1817.795			3908.093		
	MIN, MAX	1368.505, 1940.999			1222.808, 5570.650		
	5%, 95%	1368.505, 1940.999			1222.808, 5570.650		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1492.836, 1403.577			2307.101, 1960.646		
	SD, SE	719.0696, 508.4590			1338.8035, 772.9586		
	MEDIAN	1492.836			2673.704		
	MIN, MAX	984.377, 2001.295			823.186, 3424.414		
	5%, 95%	984.377, 2001.295			823.186, 3424.414		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	1721.027, 1707.001			2603.765, 2399.602		
	SD, SE	260.5469, 150.4268			1132.7438, 653.9899		
	MEDIAN	1865.747			3066.133		
	MIN, MAX	1420.245, 1877.090			1312.972, 3432.189		
	5%, 95%	1420.245, 1877.090			1312.972, 3432.189		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 214 of 264)

Biomarker: Total 3-hydroxycotinine ((ug/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	353.041, 352.906			372.293, 336.214		
	SD, SE	12.0018, 6.9293			193.3023, 111.6032		
	MEDIAN	348.301			363.820		
	MIN, MAX	344.133, 366.689			183.367, 569.693		
	5%, 95%	344.133, 366.689			183.367, 569.693		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	328.489, 324.857			685.613, 573.892		
	SD, SE	57.9149, 33.4372			421.6630, 243.4473		
	MEDIAN	349.380			751.135		
	MIN, MAX	263.027, 373.060			235.024, 1070.679		
	5%, 95%	263.027, 373.060			235.024, 1070.679		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	286.923, 269.767			443.425, 376.836		
	SD, SE	138.2054, 97.7260			257.3181, 148.5627		
	MEDIAN	286.923			513.886		
	MIN, MAX	189.197, 384.649			158.216, 658.172		
	5%, 95%	189.197, 384.649			158.216, 658.172		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	330.782, 328.086			500.444, 461.203		
	SD, SE	50.0774, 28.9122			217.7136, 125.6970		
	MEDIAN	358.597			589.311		
	MIN, MAX	272.971, 360.777			252.353, 659.667		
	5%, 95%	272.971, 360.777			252.353, 659.667		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	15.979, 14.956	0.022, 0.022		36.794, 30.430	0.031, 0.041	
	SD, SE	6.9296, 4.0008	0.0042, 0.0030		28.8498, 16.6564	0.0400, 0.0231	
	MEDIAN	15.278	0.022		22.427	0.039	
	MIN, MAX	9.426, 23.232	0.019, 0.025		17.948, 70.006	0.019, 0.096	
	5%, 95%	9.426, 23.232	0.019, 0.025		17.948, 70.006	0.019, 0.096	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0765	3	2	0.1489
	MEAN, GEO MEAN	19.232, 18.698	0.022, 0.022		38.488, 29.184	0.019, 0.017	
	SD, SE	5.6416, 3.2572	0.0064, 0.0037		35.6930, 20.6074	0.0106, 0.0075	
	MEDIAN	18.022	0.026		21.151	0.019	
	MIN, MAX	14.293, 25.380	0.015, 0.026		14.775, 79.538	0.011, 0.026	
	5%, 95%	14.293, 25.380	0.015, 0.026		14.775, 79.538	0.011, 0.026	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1489	3	2	0.1489
	MEAN, GEO MEAN	14.967, 14.298	0.021, 0.021		30.402, 21.584	0.020, 0.018	
	SD, SE	6.2579, 4.4250	0.0057, 0.0033		30.8849, 17.8314	0.0113, 0.0080	
	MEDIAN	14.967	0.023		15.321	0.020	
	MIN, MAX	10.542, 19.392	0.015, 0.026		9.955, 65.930	0.012, 0.028	
	5%, 95%	10.542, 19.392	0.015, 0.026		9.955, 65.930	0.012, 0.028	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall ^b	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	17.763, 16.956	0.022, 0.022		35.228, 27.172	0.047, 0.035	
	SD, SE	6.4453, 3.7212	0.0025, 0.0015		31.8090, 18.3650	0.0433, 0.0250	
	MEDIAN	17.564	0.022		19.633	0.031	
	MIN, MAX	11.420, 24.306	0.020, 0.025		14.226, 71.825	0.014, 0.096	
	5%, 95%	11.420, 24.306	0.020, 0.025		14.226, 71.825	0.014, 0.096	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 216 of 264)

Biomarker: Total 3-hydroxycotinine (pg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	3.071, 2.875	0.005, 0.004		7.072, 5.849	0.010, 0.008	
	SD, SE	1.3316, 0.7688	0.0007, 0.0005		5.5448, 3.2013	0.0074, 0.0043	
	MEDIAN	2.936	0.005		4.310	0.007	
	MIN, MAX	1.812, 4.465	0.004, 0.005		3.450, 13.455	0.004, 0.018	
	5%, 95%	1.812, 4.465	0.004, 0.005		3.450, 13.455	0.004, 0.018	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0765	3	2	0.1489
	MEAN, GEO MEAN	3.696, 3.594	0.004, 0.004		7.397, 5.609	0.004, 0.003	
	SD, SE	1.0843, 0.6260	0.0012, 0.0007		6.8601, 3.9607	0.0021, 0.0015	
	MEDIAN	3.464	0.005		4.065	0.004	
	MIN, MAX	2.747, 4.878	0.003, 0.005		2.840, 15.287	0.002, 0.005	
	5%, 95%	2.747, 4.878	0.003, 0.005		2.840, 15.287	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1489	3	2	0.1489
	MEAN, GEO MEAN	2.877, 2.748	0.004, 0.004		5.843, 4.148	0.004, 0.003	
	SD, SE	1.2028, 0.8505	0.0010, 0.0006		5.9363, 3.4273	0.0021, 0.0015	
	MEDIAN	2.877	0.004		2.945	0.004	
	MIN, MAX	2.026, 3.727	0.003, 0.005		1.913, 12.672	0.002, 0.005	
	5%, 95%	2.026, 3.727	0.003, 0.005		1.913, 12.672	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall ^b	N	3	3	0.0809	3	3	0.0809
	MEAN, GEO MEAN	3.414, 3.259	0.004, 0.004		6.771, 5.222	0.009, 0.007	
	SD, SE	1.2389, 0.7153	0.0006, 0.0003		6.1140, 3.5299	0.0079, 0.0046	
	MEDIAN	3.376	0.004		3.773	0.006	
	MIN, MAX	2.195, 4.672	0.004, 0.005		2.734, 13.805	0.003, 0.018	
	5%, 95%	2.195, 4.672	0.004, 0.005		2.734, 13.805	0.003, 0.018	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 217 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1.285, 1.264			1.726, 1.334		
	SD, SE	0.2807, 0.1621			1.5448, 0.8919		
	MEDIAN	1.273			0.997		
	MIN, MAX	1.010, 1.571			0.680, 3.500		
	5%, 95%	1.010, 1.571			0.680, 3.500		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1.445, 1.437			2.747, 2.180		
	SD, SE	0.1850, 0.1068			1.7536, 1.0124		
	MEDIAN	1.429			3.525		
	MIN, MAX	1.269, 1.638			0.739, 3.977		
	5%, 95%	1.269, 1.638			0.739, 3.977		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1.687, 1.685			2.135, 1.670		
	SD, SE	0.0997, 0.0705			1.4192, 0.8194		
	MEDIAN	1.687			2.554		
	MIN, MAX	1.616, 1.757			0.553, 3.297		
	5%, 95%	1.616, 1.757			0.553, 3.297		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	1.412, 1.397			2.202, 1.834		
	SD, SE	0.2384, 0.1376			1.4147, 0.8168		
	MEDIAN	1.509			2.253		
	MIN, MAX	1.140, 1.586			0.763, 3.591		
	5%, 95%	1.140, 1.586			0.763, 3.591		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 218 of 264)

Biomarker: Total 3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.247, 0.243			0.332, 0.257		
	SD, SE	0.0540, 0.0312			0.2969, 0.1714		
	MEDIAN	0.245			0.192		
	MIN, MAX	0.194, 0.302			0.131, 0.673		
	5%, 95%	0.194, 0.302			0.131, 0.673		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.278, 0.276			0.528, 0.419		
	SD, SE	0.0356, 0.0206			0.3370, 0.1946		
	MEDIAN	0.275			0.678		
	MIN, MAX	0.244, 0.315			0.142, 0.764		
	5%, 95%	0.244, 0.315			0.142, 0.764		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.325, 0.324			0.410, 0.321		
	SD, SE	0.0191, 0.0135			0.2731, 0.1577		
	MEDIAN	0.325			0.491		
	MIN, MAX	0.311, 0.338			0.106, 0.634		
	5%, 95%	0.311, 0.338			0.106, 0.634		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.271, 0.269			0.423, 0.353		
	SD, SE	0.0459, 0.0265			0.2716, 0.1568		
	MEDIAN	0.290			0.433		
	MIN, MAX	0.219, 0.305			0.147, 0.690		
	5%, 95%	0.219, 0.305			0.147, 0.690		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 219 of 264)

Biomarker: Total 3-hydroxycotinine (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	2	0.1489	3	3	0.0765
	MEAN, GEO MEAN	19663.7, 17523.9	28.5, 23.5		17857.8, 17465.3	21.9, 18.5	
	SD, SE	9744.29, 5625.87	22.70, 16.05		4337.31, 2504.15	16.45, 9.50	
	MEDIAN	24995.6	28.5		20281.3	12.4	
	MIN, MAX	8417.0, 25578.5	12.4, 44.5		12850.4, 20441.8	12.4, 40.9	
	5%, 95%	8417.0, 25578.5	12.4, 44.5		12850.4, 20441.8	12.4, 40.9	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0765	3	2	0.1386
	MEAN, GEO MEAN	22250.3, 18298.4	22.2, 18.6		17703.7, 16917.1	12.4, 12.4	
	SD, SE	15078.23, 8705.42	17.03, 9.83		6696.93, 3866.47	0.00, 0.00	
	MEDIAN	21500.8	12.4		15546.0	12.4	
	MIN, MAX	7560.8, 37689.3	12.4, 41.9		12351.6, 25213.5	12.4, 12.4	
	5%, 95%	7560.8, 37689.3	12.4, 41.9		12351.6, 25213.5	12.4, 12.4	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1066	3	2	0.1386
	MEAN, GEO MEAN	9886.9, 8143.2	12.4, 12.4		14951.2, 12532.8	12.4, 12.4	
	SD, SE	7929.50, 5607.00	0.00, 0.00		11304.34, 6526.57	0.00, 0.00	
	MEDIAN	9886.9	12.4		9437.8	12.4	
	MIN, MAX	4279.9, 15493.9	12.4, 12.4		7461.5, 27954.4	12.4, 12.4	
	5%, 95%	4279.9, 15493.9	12.4, 12.4		7461.5, 27954.4	12.4, 12.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall ^b	N	3	3	0.0765	3	3	0.0765
	MEAN, GEO MEAN	19683.3, 16403.7	19.2, 17.2		16837.6, 16021.8	21.9, 18.5	
	SD, SE	12469.57, 7199.31	11.84, 6.83		6747.46, 3895.65	16.45, 9.50	
	MEDIAN	20663.4	12.4		14023.6	12.4	
	MIN, MAX	6752.6, 31633.9	12.4, 32.9		11952.6, 24536.6	12.4, 40.9	
	5%, 95%	6752.6, 31633.9	12.4, 32.9		11952.6, 24536.6	12.4, 40.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 220 of 264)

Biomarker: Total 3-hydroxycotinine (ng/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value*	Smokers	Female Non-Smokers	P-value*
Week 1	N	3	2	0.1489	3	3	0.0765
	MEAN, GEO MEAN	3779.4, 3368.1	5.5, 4.5		3432.3, 3356.8	4.2, 3.6	
	SD, SE	1872.90, 1081.32	4.38, 3.10		833.66, 481.32	3.18, 1.83	
	MEDIAN	4804.2	5.5		3898.1	2.4	
	MIN, MAX	1617.7, 4916.2	2.4, 8.6		2469.8, 3928.9	2.4, 7.9	
	5%, 95%	1617.7, 4916.2	2.4, 8.6		2469.8, 3928.9	2.4, 7.9	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	3	0.0765	3	2	0.1386
	MEAN, GEO MEAN	4276.5, 3517.0	4.3, 3.6		3402.6, 3251.4	2.4, 2.4	
	SD, SE	2898.04, 1673.18	3.29, 1.90		1287.13, 743.12	0.00, 0.00	
	MEDIAN	4132.5	2.4		2987.9	2.4	
	MIN, MAX	1453.2, 7243.9	2.4, 8.1		2374.0, 4846.0	2.4, 2.4	
	5%, 95%	1453.2, 7243.9	2.4, 8.1		2374.0, 4846.0	2.4, 2.4	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	3	0.1066	3	2	0.1386
	MEAN, GEO MEAN	1900.3, 1565.1	2.4, 2.4		2873.6, 2408.8	2.4, 2.4	
	SD, SE	1524.03, 1077.65	0.00, 0.00		2172.69, 1254.40	0.00, 0.00	
	MEDIAN	1900.3	2.4		1813.9	2.4	
	MIN, MAX	822.6, 2977.9	2.4, 2.4		1434.1, 5372.8	2.4, 2.4	
	5%, 95%	822.6, 2977.9	2.4, 2.4		1434.1, 5372.8	2.4, 2.4	
	# of BLQ/ALQ Values	0/0	3/0		0/0	2/0	
Overall†	N	3	3	0.0765	3	3	0.0765
	MEAN, GEO MEAN	3783.1, 3152.8	3.7, 3.3		3236.2, 3079.4	4.2, 3.6	
	SD, SE	2396.71, 1383.74	2.31, 1.33		1296.85, 748.73	3.18, 1.83	
	MEDIAN	3971.5	2.4		2695.3	2.4	
	MIN, MAX	1297.8, 6080.1	2.4, 6.4		2297.3, 4715.9	2.4, 7.9	
	5%, 95%	1297.8, 6080.1	2.4, 6.4		2297.3, 4715.9	2.4, 7.9	

* P-value from Wilcoxon rank-sum test.

† Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234 will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 221 of 264)

Biomarker: Total 3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1532.6, 1481.2			846.1, 765.4		
	SD, SE	498.30, 287.69			398.93, 230.32		
	MEDIAN	1402.8			1022.1		
	MIN, MAX	1112.1, 2083.0			389.4, 1126.7		
	5%, 95%	1112.1, 2083.0			389.4, 1126.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1531.7, 1406.9			1489.8, 1263.6		
	SD, SE	672.63, 388.34			1006.44, 581.07		
	MEDIAN	1884.5			1260.7		
	MIN, MAX	756.1, 1954.6			617.6, 2591.0		
	5%, 95%	756.1, 1954.6			617.6, 2591.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1002.3, 959.7			1055.2, 969.5		
	SD, SE	408.64, 288.95			466.18, 269.15		
	MEDIAN	1002.3			1243.6		
	MIN, MAX	713.3, 1291.2			524.3, 1397.7		
	5%, 95%	713.3, 1291.2			524.3, 1397.7		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1410.7, 1365.8			1130.3, 1093.1		
	SD, SE	416.42, 240.42			336.44, 194.24		
	MEDIAN	1498.3			1226.8		
	MIN, MAX	957.4, 1776.3			756.2, 1408.0		
	5%, 95%	957.4, 1776.3			756.2, 1408.0		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as 1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total 3-hydroxycotinine ((ng/mL)/cigarette per day)			Analytical Lab: INBIFO				
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	294.6, 284.7			162.6, 147.1		
	SD, SE	95.82, 55.32			76.70, 44.29		
	MEDIAN	269.6			196.4		
	MIN, MAX	213.7, 400.4			74.8, 216.6		
	5%, 95%	213.7, 400.4			74.8, 216.6		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	294.4, 270.4			286.3, 242.9		
	SD, SE	129.30, 74.65			193.45, 111.69		
	MEDIAN	362.2			242.3		
	MIN, MAX	145.3, 375.7			118.7, 498.0		
	5%, 95%	145.3, 375.7			118.7, 498.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	192.7, 184.5			202.8, 186.3		
	SD, SE	78.56, 55.55			89.57, 51.71		
	MEDIAN	192.7			239.0		
	MIN, MAX	137.1, 248.2			100.8, 268.6		
	5%, 95%	137.1, 248.2			100.8, 268.6		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	271.1, 262.5			217.3, 210.1		
	SD, SE	80.04, 46.21			64.62, 37.31		
	MEDIAN	288.0			235.8		
	MIN, MAX	184.0, 341.4			145.4, 270.6		
	5%, 95%	184.0, 341.4			145.4, 270.6		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Draft 1: 24 July 2002

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	3	4	0.0518	3	2	0.1489
	MEAN, GEO MEAN	20519.870, 14594.558	21.588, 20.493		22557.729, 21545.646	24.244, 21.582	
	SD, SE	15520.0834, 8960.5243	8.3176, 4.1588		8433.2883, 4868.9613	15.6186, 11.0440	
	MEDIAN	23030.245	19.360		20668.880	24.244	
	MIN, MAX	3897.624, 34631.742	14.630, 33.000		15229.032, 31775.275	13.200, 35.288	
	5%, 95%	3897.624, 34631.742	14.630, 33.000		15229.032, 31775.275	13.200, 35.288	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0497	3	3	0.0809
	MEAN, GEO MEAN	19603.498, 16623.663	24.778, 23.960		24282.046, 23632.999	26.822, 23.829	
	SD, SE	11343.7587, 6549.3222	7.3029, 3.6514		6492.8975, 3748.6761	13.6303, 7.8694	
	MEDIAN	23208.990	24.365		26974.030	31.625	
	MIN, MAX	6895.195, 28706.310	18.480, 31.900		16876.134, 28995.975	11.440, 37.400	
	5%, 95%	6895.195, 28706.310	18.480, 31.900		16876.134, 28995.975	11.440, 37.400	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	16931.545, 8752.583	26.604, 26.029		19312.086, 18375.629	16.903, 16.673	
	SD, SE	20497.2932, 14493.7750	6.2922, 3.1461		6996.4999, 4039.4311	3.4686, 2.0026	
	MEDIAN	16931.545	27.302		20410.460	16.170	
	MIN, MAX	2437.770, 31425.320	19.800, 32.010		11831.363, 25694.435	13.860, 20.680	
	5%, 95%	2437.770, 31425.320	19.800, 32.010		11831.363, 25694.435	13.860, 20.680	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	19705.868, 14767.918	24.323, 23.769		22050.621, 21234.978	22.875, 21.190	
	SD, SE	13906.6776, 8029.0241	6.0605, 3.0302		7109.4152, 4104.6228	9.9295, 4.9647	
	MEDIAN	23119.618	23.467		22684.457	22.605	
	MIN, MAX	4410.196, 31587.791	18.605, 31.753		14645.510, 28821.895	12.833, 33.457	
	5%, 95%	4410.196, 31587.791	18.605, 31.753		14645.510, 28821.895	12.833, 33.457	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 224 of 264)

Biomarker: Total Cotinine (µg/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0518	3	2	0.1489
	MEAN, GEO MEAN	3615.601, 2571.561	3.804, 3.611		3974.672, 3796.343	4.272, 3.803	
	SD, SE	2734.6389, 1578.8445	1.4656, 0.7328		1485.9453, 857.9109	2.7521, 1.9460	
	MEDIAN	4057.929	3.412		3641.857	4.272	
	MIN, MAX	686.761, 6102.113	2.578, 5.815		2683.355, 5598.803	2.326, 6.218	
	5%, 95%	686.761, 6102.113	2.578, 5.815		2683.355, 5598.803	2.326, 6.218	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0497	3	3	0.0809
	MEAN, GEO MEAN	3454.136, 2929.089	4.366, 4.222		4278.497, 4164.135	4.726, 4.199	
	SD, SE	1998.7706, 1153.9907	1.2869, 0.6435		1144.0485, 660.5167	2.4015, 1.3865	
	MEDIAN	4089.424	4.293		4752.824	5.572	
	MIN, MAX	1214.933, 5058.052	3.256, 5.621		2973.575, 5109.091	2.016, 6.590	
	5%, 95%	1214.933, 5058.052	3.256, 5.621		2973.575, 5109.091	2.016, 6.590	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	2983.338, 1542.205	4.688, 4.586		3402.789, 3237.786	2.978, 2.938	
	SD, SE	3611.6228, 2553.8030	1.1087, 0.5544		1232.7832, 711.7477	0.6113, 0.3530	
	MEDIAN	2983.338	4.811		3596.323	2.849	
	MIN, MAX	429.535, 5537.141	3.489, 5.640		2084.686, 4527.359	2.442, 3.644	
	5%, 95%	429.535, 5537.141	3.489, 5.640		2084.686, 4527.359	2.442, 3.644	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	3472.174, 2602.107	4.286, 4.188		3885.319, 3741.603	4.031, 3.734	
	SD, SE	2450.3570, 1414.7143	1.0681, 0.5341		1252.6789, 723.2345	1.7497, 0.8748	
	MEDIAN	4073.677	4.135		3997.001	3.983	
	MIN, MAX	777.076, 5565.769	3.278, 5.595		2580.539, 5078.418	2.261, 5.895	
	5%, 95%	777.076, 5565.769	3.278, 5.595		2580.539, 5078.418	2.261, 5.895	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 225 of 264)

Biomarker: Total Cotinine ((nmol/24hr)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1512.299, 1233.590			947.463, 944.251		
	SD, SE	1202.5689, 694.3035			94.6409, 54.6410		
	MEDIAN	1001.315			962.887		
	MIN, MAX	649.604, 2885.979			846.057, 1033.444		
	5%, 95%	649.604, 2885.979			846.057, 1033.444		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1486.545, 1278.162			2341.724, 1765.151		
	SD, SE	1000.7461, 577.7810			2171.9375, 1253.9687		
	MEDIAN	1160.450			1348.702		
	MIN, MAX	689.520, 2609.665			843.807, 4832.663		
	5%, 95%	689.520, 2609.665			843.807, 4832.663		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1512.536, 1031.502			1986.742, 1421.535		
	SD, SE	1564.4610, 1106.2410			1996.3809, 1152.6111		
	MEDIAN	1512.536			1020.523		
	MIN, MAX	406.295, 2618.777			657.298, 4282.406		
	5%, 95%	406.295, 2618.777			657.298, 4282.406		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1455.832, 1193.707			1758.643, 1439.209		
	SD, SE	1110.0556, 640.8909			1397.3439, 806.7569		
	MEDIAN	1080.883			1134.223		
	MIN, MAX	581.806, 2704.807			782.387, 3359.319		
	5%, 95%	581.806, 2704.807			782.387, 3359.319		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 226 of 264)

Biomarker: Total Cotinine ((µg/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	266.467, 217.358			166.943, 166.377		
	SD, SE	211.8924, 122.3361			16.6760, 9.6279		
	MEDIAN	176.432			169.661		
	MIN, MAX	114.460, 508.509			149.075, 182.093		
	5%, 95%	114.460, 508.509			149.075, 182.093		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	261.929, 225.212			412.612, 311.020		
	SD, SE	176.3317, 101.8051			382.6953, 220.9492		
	MEDIAN	204.471			237.641		
	MIN, MAX	121.493, 459.823			148.679, 851.515		
	5%, 95%	121.493, 459.823			148.679, 851.515		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	266.509, 181.750			350.064, 250.475		
	SD, SE	275.6578, 194.9195			351.7624, 203.0901		
	MEDIAN	266.509			179.816		
	MIN, MAX	71.589, 461.428			115.816, 754.560		
	5%, 95%	71.589, 461.428			115.816, 754.560		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	256.518, 210.331			309.873, 253.589		
	SD, SE	195.5918, 112.9250			246.2119, 142.1505		
	MEDIAN	190.452			199.850		
	MIN, MAX	102.514, 476.587			137.857, 591.912		
	5%, 95%	102.514, 476.587			137.857, 591.912		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Cotinine (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0318	3	2	0.1489
	MEAN, GEO MEAN	13.511, 10.048	0.011, 0.010		18.355, 16.426	0.026, 0.024	
	SD, SE	10.5711, 6.1032	0.0048, 0.0024		8.9922, 5.1917	0.0120, 0.0085	
	MEDIAN	12.992	0.011		22.634	0.026	
	MIN, MAX	3.209, 24.332	0.006, 0.017		8.022, 24.408	0.017, 0.034	
	5%, 95%	3.209, 24.332	0.006, 0.017		8.022, 24.408	0.017, 0.034	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	16.083, 14.140	0.014, 0.013		18.664, 17.252	0.023, 0.020	
	SD, SE	9.3691, 5.4093	0.0066, 0.0033		8.6313, 4.9833	0.0145, 0.0084	
	MEDIAN	15.174	0.014		18.349	0.023	
	MIN, MAX	7.201, 25.873	0.007, 0.023		10.195, 27.449	0.009, 0.038	
	5%, 95%	7.201, 25.873	0.007, 0.023		10.195, 27.449	0.009, 0.038	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	14.863, 10.507	0.018, 0.017		17.379, 15.650	0.018, 0.017	
	SD, SE	14.8662, 10.5120	0.0050, 0.0025		8.5251, 4.9219	0.0064, 0.0037	
	MEDIAN	14.863	0.018		19.648	0.021	
	MIN, MAX	4.351, 25.375	0.013, 0.023		7.949, 24.540	0.011, 0.023	
	5%, 95%	4.351, 25.375	0.013, 0.023		7.949, 24.540	0.011, 0.023	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0497	3	4	0.0518
	MEAN, GEO MEAN	14.732, 12.041	0.015, 0.014		18.133, 16.559	0.024, 0.022	
	SD, SE	10.1521, 5.8613	0.0043, 0.0021		8.2106, 4.7404	0.0083, 0.0041	
	MEDIAN	14.083	0.016		21.841	0.026	
	MIN, MAX	4.920, 25.193	0.009, 0.018		8.722, 23.835	0.012, 0.030	
	5%, 95%	4.920, 25.193	0.009, 0.018		8.722, 23.835	0.012, 0.030	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 228 of 264)

Biomarker: Total Cotinine (µg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0497	3	2	0.1489
	MEAN, GEO MEAN	2.380, 1.770	0.002, 0.002		3.234, 2.894	0.005, 0.004	
	SD, SE	1.8627, 1.0754	0.0008, 0.0004		1.5848, 0.9150	0.0021, 0.0015	
	MEDIAN	2.289	0.002		3.988	0.005	
	MIN, MAX	0.565, 4.287	0.001, 0.003		1.413, 4.301	0.003, 0.006	
	5%, 95%	0.565, 4.287	0.001, 0.003		1.413, 4.301	0.003, 0.006	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0497	3	3	0.0809
	MEAN, GEO MEAN	2.834, 2.492	0.002, 0.002		3.289, 3.040	0.004, 0.004	
	SD, SE	1.6508, 0.9531	0.0013, 0.0006		1.5213, 0.8783	0.0025, 0.0015	
	MEDIAN	2.674	0.002		3.233	0.004	
	MIN, MAX	1.269, 4.559	0.001, 0.004		1.796, 4.837	0.002, 0.007	
	5%, 95%	1.269, 4.559	0.001, 0.004		1.796, 4.837	0.002, 0.007	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.0952	3	3	0.0765
	MEAN, GEO MEAN	2.619, 1.852	0.003, 0.003		3.062, 2.758	0.003, 0.003	
	SD, SE	2.6191, 1.8520	0.0012, 0.0006		1.5019, 0.8671	0.0012, 0.0007	
	MEDIAN	2.619	0.003		3.462	0.004	
	MIN, MAX	0.767, 4.471	0.002, 0.004		1.401, 4.324	0.002, 0.004	
	5%, 95%	0.767, 4.471	0.002, 0.004		1.401, 4.324	0.002, 0.004	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	2.596, 2.122	0.002, 0.002		3.195, 2.918	0.004, 0.004	
	SD, SE	1.7887, 1.0327	0.0010, 0.0005		1.4466, 0.8352	0.0017, 0.0009	
	MEDIAN	2.482	0.003		3.848	0.005	
	MIN, MAX	0.867, 4.439	0.001, 0.003		1.537, 4.200	0.002, 0.006	
	5%, 95%	0.867, 4.439	0.001, 0.003		1.537, 4.200	0.002, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 229 of 264)

Biomarker: Total Cotinine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	1.043, 0.849			0.784, 0.720	
	SD, SE	0.8535, 0.4927			0.3962, 0.2287	
	MEDIAN	0.565			0.686	
	MIN, MAX	0.535, 2.028			0.446, 1.220	
	5%, 95%	0.535, 2.028			0.446, 1.220	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	1.277, 1.087			1.647, 1.289	
	SD, SE	0.9312, 0.5376			1.2960, 0.7483	
	MEDIAN	0.759			1.372	
	MIN, MAX	0.720, 2.352			0.510, 3.058	
	5%, 95%	0.720, 2.352			0.510, 3.058	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	1.420, 1.238			1.838, 1.211	
	SD, SE	0.9829, 0.6950			1.9689, 1.1367	
	MEDIAN	1.420			0.982	
	MIN, MAX	0.725, 2.115			0.442, 4.090	
	5%, 95%	0.725, 2.115			0.442, 4.090	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	1.162, 0.982			1.423, 1.132	
	SD, SE	0.8683, 0.5013			1.0911, 0.6299	
	MEDIAN	0.662			1.191	
	MIN, MAX	0.660, 2.165			0.466, 2.611	
	5%, 95%	0.660, 2.165			0.466, 2.611	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439397

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 230 of 264)

Biomarker: Total Cotinine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	0.184, 0.150			0.138, 0.127	
	SD, SE	0.1501, 0.0867			0.0696, 0.0402	
	MEDIAN	0.100			0.121	
	MIN, MAX	0.094, 0.357			0.079, 0.215	
	5%, 95%	0.094, 0.357			0.079, 0.215	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	0.225, 0.192			0.290, 0.227	
	SD, SE	0.1637, 0.0945			0.2284, 0.1318	
	MEDIAN	0.134			0.242	
	MIN, MAX	0.127, 0.414			0.090, 0.539	
	5%, 95%	0.127, 0.414			0.090, 0.539	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	0.251, 0.219			0.324, 0.213	
	SD, SE	0.1732, 0.1225			0.3471, 0.2004	
	MEDIAN	0.251			0.173	
	MIN, MAX	0.128, 0.373			0.078, 0.721	
	5%, 95%	0.128, 0.373			0.078, 0.721	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	0.205, 0.173			0.251, 0.199	
	SD, SE	0.1527, 0.0882			0.1923, 0.1110	
	MEDIAN	0.117			0.210	
	MIN, MAX	0.116, 0.381			0.082, 0.460	
	5%, 95%	0.116, 0.381			0.082, 0.460	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

PM3006439398

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 231 of 264)

Biomarker: Total Cotinine (nmol/L) Analytical Lab: INBIFO		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	3	4	0.0319	3	2	0.1386
	MEAN, GEO MEAN	18992.3, 11773.2	11.0, 11.0		9720.5, 9427.6	11.0, 11.0	
	SD, SE	18911.26, 10918.42	0.00, 0.00		2975.82, 1718.09	0.00, 0.00	
	MEDIAN	14304.5	11.0		9064.9	11.0	
	MIN, MAX	2865.9, 39806.6	11.0, 11.0		7127.2, 12969.5	11.0, 11.0	
	5%, 95%	2865.9, 39806.6	11.0, 11.0		7127.2, 12969.5	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0319	3	3	0.0636
	MEAN, GEO MEAN	19069.8, 13837.6	11.0, 11.0		10237.0, 10000.7	11.0, 11.0	
	SD, SE	13857.21, 8000.46	0.00, 0.00		2815.53, 1625.55	0.00, 0.00	
	MEDIAN	22533.0	11.0		8701.3	11.0	
	MIN, MAX	3809.5, 30867.0	11.0, 11.0		8523.3, 13486.5	11.0, 11.0	
	5%, 95%	3809.5, 30867.0	11.0, 11.0		8523.3, 13486.5	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.0552	3	3	0.0636
	MEAN, GEO MEAN	11020.5, 5984.5	11.0, 11.0		9272.5, 9086.7	11.0, 11.0	
	SD, SE	13087.06, 9253.95	0.00, 0.00		2353.34, 1358.70	0.00, 0.00	
	MEDIAN	11020.5	11.0		8330.8	11.0	
	MIN, MAX	1766.5, 20274.4	11.0, 11.0		7535.9, 11950.9	11.0, 11.0	
	5%, 95%	1766.5, 20274.4	11.0, 11.0		7535.9, 11950.9	11.0, 11.0	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall*	N	3	4	0.0319	3	4	0.0319
	MEAN, GEO MEAN	17182.9, 11625.7	11.0, 11.0		9743.4, 9522.3	11.0, 11.0	
	SD, SE	13792.59, 7963.16	0.00, 0.00		2653.99, 1532.28	0.00, 0.00	
	MEDIAN	18418.8	11.0		8374.7	11.0	
	MIN, MAX	2814.0, 30316.0	11.0, 11.0		8053.1, 12802.3	11.0, 11.0	
	5%, 95%	2814.0, 30316.0	11.0, 11.0		8053.1, 12802.3	11.0, 11.0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439399

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 232 of 264)

Biomarker: Total Cotinine (ng/mL) Analytical Lab: INBIFO		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0319	3	2	0.1386
	MEAN, GEO MEAN	3346.5, 2074.5	1.9, 1.9		1712.7, 1661.1	1.9, 1.9	
	SD, SE	3332.13, 1923.81	0.00, 0.00		524.33, 302.72	0.00, 0.00	
	MEDIAN	2520.5	1.9		1597.2	1.9	
	MIN, MAX	505.0, 7013.9	1.9, 1.9		1255.8, 2285.2	1.9, 1.9	
	5%, 95%	505.0, 7013.9	1.9, 1.9		1255.8, 2285.2	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	4/0		0/0	2/0	
Week 2	N	3	4	0.0319	3	3	0.0636
	MEAN, GEO MEAN	3360.1, 2438.1	1.9, 1.9		1803.8, 1762.1	1.9, 1.9	
	SD, SE	2441.67, 1409.70	0.00, 0.00		496.08, 286.41	0.00, 0.00	
	MEDIAN	3970.3	1.9		1533.2	1.9	
	MIN, MAX	671.2, 5438.8	1.9, 1.9		1501.8, 2376.3	1.9, 1.9	
	5%, 95%	671.2, 5438.8	1.9, 1.9		1501.8, 2376.3	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Week 3	N	2	4	0.0552	3	3	0.0636
	MEAN, GEO MEAN	1941.8, 1054.5	1.9, 1.9		1633.8, 1601.1	1.9, 1.9	
	SD, SE	2305.88, 1630.50	0.00, 0.00		414.64, 239.39	0.00, 0.00	
	MEDIAN	1941.8	1.9		1467.9	1.9	
	MIN, MAX	311.3, 3572.3	1.9, 1.9		1327.8, 2105.7	1.9, 1.9	
	5%, 95%	311.3, 3572.3	1.9, 1.9		1327.8, 2105.7	1.9, 1.9	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0319	3	4	0.0319
	MEAN, GEO MEAN	3027.6, 2048.4	1.9, 1.9		1716.8, 1677.8	1.9, 1.9	
	SD, SE	2430.28, 1403.12	0.00, 0.00		467.59, 269.96	0.00, 0.00	
	MEDIAN	3245.4	1.9		1475.6	1.9	
	MIN, MAX	495.8, 5341.7	1.9, 1.9		1419.0, 2255.7	1.9, 1.9	
	5%, 95%	495.8, 5341.7	1.9, 1.9		1419.0, 2255.7	1.9, 1.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439400

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 233 of 264)

Biomarker: Total Cotinine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1472.3, 995.1			417.7, 413.2		
	SD, SE	1599.39, 923.41			76.64, 44.25		
	MEDIAN	621.9			393.0		
	MIN, MAX	477.7, 3317.2			356.4, 503.6		
	5%, 95%	477.7, 3317.2			356.4, 503.6		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1437.9, 1064.0			1036.4, 747.0		
	SD, SE	1242.15, 717.15			1049.14, 605.72		
	MEDIAN	1126.7			435.1		
	MIN, MAX	381.0, 2806.1			426.2, 2247.8		
	5%, 95%	381.0, 2806.1			426.2, 2247.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	992.0, 705.3			942.3, 702.9		
	SD, SE	986.48, 697.55			908.87, 524.73		
	MEDIAN	992.0			418.7		
	MIN, MAX	294.4, 1689.5			416.5, 1991.8		
	5%, 95%	294.4, 1689.5			416.5, 1991.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1287.7, 956.6			798.8, 653.8		
	SD, SE	1166.25, 673.34			645.96, 372.94		
	MEDIAN	874.3			449.5		
	MIN, MAX	384.4, 2604.3			402.7, 1544.2		
	5%, 95%	384.4, 2604.3			402.7, 1544.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439401

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 234 of 264)

Biomarker: Total Cotinine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	259.4, 175.4			73.6, 72.8		
	SD, SE	281.80, 162.70			13.49, 7.79		
	MEDIAN	109.6			69.2		
	MIN, MAX	84.2, 584.5			62.8, 88.7		
	5%, 95%	84.2, 584.5			62.8, 88.7		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	253.3, 187.4			182.6, 131.6		
	SD, SE	218.86, 126.36			184.87, 106.73		
	MEDIAN	198.5			76.7		
	MIN, MAX	67.1, 494.4			75.1, 396.1		
	5%, 95%	67.1, 494.4			75.1, 396.1		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	174.8, 124.3			166.1, 123.9		
	SD, SE	173.81, 122.90			160.16, 92.47		
	MEDIAN	174.8			73.8		
	MIN, MAX	51.9, 297.7			73.4, 351.0		
	5%, 95%	51.9, 297.7			73.4, 351.0		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	226.9, 168.5			140.8, 115.2		
	SD, SE	205.51, 118.65			113.81, 65.71		
	MEDIAN	154.1			79.2		
	MIN, MAX	67.7, 458.9			71.0, 272.1		
	5%, 95%	67.7, 458.9			71.0, 272.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439402

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 235 of 264)

Biomarker: Total Nicotine (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	18044.438, 14878.493	38.100, 38.100		8635.728, 8049.119	27.991, 24.918	
	SD, SE	10825.1649, 6249.9118	NA, NA		4082.2773, 2356.9030	18.0326, 12.7510	
	MEDIAN	23200.422	38.100		7159.230	27.991	
	MIN, MAX	5605.104, 25327.788	38.100, 38.100		5497.128, 13250.825	15.240, 40.742	
	5%, 95%	5605.104, 25327.788	NA, NA		5497.128, 13250.825	15.240, 40.742	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	13631.052, 12261.172	35.878, 35.865		11106.904, 10275.592	43.690, 43.268	
	SD, SE	6848.8611, 3954.1918	1.3470, 0.9525		5507.3989, 3179.6983	7.4446, 4.2981	
	MEDIAN	14725.704	35.878		9159.570	43.180	
	MIN, MAX	6300.791, 19866.660	34.925, 36.830		6837.732, 17323.410	36.513, 51.376	
	5%, 95%	6300.791, 19866.660	34.925, 36.830		6837.732, 17323.410	36.513, 51.376	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	8440.238, 6209.580	30.715, 30.052		10011.533, 9589.062	26.839, 24.948	
	SD, SE	8084.3971, 5716.5320	7.2646, 3.6323		3639.1714, 2101.0766	12.5835, 7.2651	
	MEDIAN	8440.238	31.522		9143.680	23.876	
	MIN, MAX	2723.706, 14156.770	22.860, 36.957		6884.745, 14006.175	16.002, 40.640	
	5%, 95%	2723.706, 14156.770	22.860, 36.957		6884.745, 14006.175	16.002, 40.640	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	14541.112, 12230.458	30.641, 29.992		9918.055, 9370.867	33.455, 33.106	
	SD, SE	8379.8227, 4838.0929	7.1809, 3.5904		4289.6139, 2476.6098	5.8798, 3.3947	
	MEDIAN	18963.063	31.437		7734.515	33.528	
	MIN, MAX	4876.534, 19783.739	22.860, 36.830		7159.513, 14860.137	27.539, 39.298	
	5%, 95%	4876.534, 19783.739	22.860, 36.830		7159.513, 14860.137	27.539, 39.298	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 236 of 264)

Biomarker: Total Nicotine (ug/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	2926.808, 2413.292	6.180, 6.180		1400.715, 1305.567	4.540, 4.042	
	SD, SE	1755.8415, 1013.7356	NA, NA		662.1456, 382.2899	2.9246, 2.0680	
	MEDIAN	3763.108	6.180		1161.227	4.540	
	MIN, MAX	909.148, 4108.167	6.180, 6.180		891.634, 2149.284	2.472, 6.608	
	5%, 95%	909.148, 4108.167	NA, NA		891.634, 2149.284	2.472, 6.608	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	2210.956, 1988.762	5.820, 5.817		1801.540, 1666.701	7.086, 7.018	
	SD, SE	1110.8853, 641.3699	0.2185, 0.1545		893.3001, 515.7471	1.2076, 0.6972	
	MEDIAN	2388.509	5.820		1485.682	7.004	
	MIN, MAX	1021.988, 3222.372	5.665, 5.974		1109.080, 2809.857	5.922, 8.333	
	5%, 95%	1021.988, 3222.372	5.665, 5.974		1109.080, 2809.857	5.922, 8.333	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	1369.007, 1007.194	4.982, 4.874		1623.871, 1555.346	4.354, 4.047	
	SD, SE	1311.2892, 927.2215	1.1782, 0.5891		590.2737, 340.7947	2.0409, 1.1783	
	MEDIAN	1369.007	5.113		1483.105	3.873	
	MIN, MAX	441.785, 2296.228	3.708, 5.994		1116.706, 2271.802	2.596, 6.592	
	5%, 95%	441.785, 2296.228	3.708, 5.994		1116.706, 2271.802	2.596, 6.592	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	2358.568, 1983.780	4.970, 4.865		1608.708, 1519.955	5.427, 5.370	
	SD, SE	1359.2070, 784.7385	1.1646, 0.5823		695.7753, 401.7061	0.9536, 0.5505	
	MEDIAN	3075.809	5.099		1254.538	5.439	
	MIN, MAX	790.974, 3208.922	3.708, 5.974		1161.273, 2410.314	4.467, 6.374	
	5%, 95%	790.974, 3208.922	3.708, 5.974		1161.273, 2410.314	4.467, 6.374	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1351.182, 1257.589			354.966, 352.758		
	SD, SE	658.7723, 380.3423			48.1420, 27.7948		
	MEDIAN	1008.714			357.962		
	MIN, MAX	934.184, 2110.649			305.396, 401.540		
	5%, 95%	934.184, 2110.649			305.396, 401.540		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1057.475, 942.738			1229.034, 767.485		
	SD, SE	650.4652, 375.5462			1437.2171, 829.7777		
	MEDIAN	736.285			457.979		
	MIN, MAX	630.079, 1806.060			341.887, 2887.235		
	5%, 95%	630.079, 1806.060			341.887, 2887.235		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	816.841, 731.806			1062.194, 741.808		
	SD, SE	513.2040, 362.8900			1104.7686, 637.8384		
	MEDIAN	816.841			507.982		
	MIN, MAX	453.951, 1179.731			344.237, 2334.363		
	5%, 95%	453.951, 1179.731			344.237, 2334.363		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1081.350, 999.046			882.064, 653.542		
	SD, SE	543.9865, 314.0708			859.3701, 496.1576		
	MEDIAN	872.500			386.726		
	MIN, MAX	672.738, 1698.813			385.088, 1874.379		
	5%, 95%	672.738, 1698.813			385.088, 1874.379		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 238 of 264)

Biomarker: Total Nicotine ((μ g/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	219.162, 203.981			57.575, 57.217		
	SD, SE	106.8527, 61.6914			7.8088, 4.5084		
	MEDIAN	153.613			58.061		
	MIN, MAX	151.525, 342.347			49.535, 65.130		
	5%, 95%	151.525, 342.347			49.535, 65.130		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	171.522, 152.912			199.349, 124.486		
	SD, SE	105.5055, 60.9136			233.1170, 134.5901		
	MEDIAN	119.425			74.284		
	MIN, MAX	102.199, 292.943			55.454, 468.310		
	5%, 95%	102.199, 292.943			55.454, 468.310		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	132.492, 118.699			172.288, 120.321		
	SD, SE	83.2413, 58.8605			179.1936, 103.4575		
	MEDIAN	132.492			82.395		
	MIN, MAX	73.631, 191.352			55.835, 378.634		
	5%, 95%	73.631, 191.352			55.835, 378.634		
	# of BLQ/ALQ Values	0/0			0/0		
Overall*	N	3		NA	3		NA
	MEAN, GEO MEAN	175.395, 162.045			143.071, 106.004		
	SD, SE	88.2345, 50.9422			139.3903, 80.4770		
	MEDIAN	141.519			62.727		
	MIN, MAX	109.118, 275.547			62.461, 304.025		
	5%, 95%	109.118, 275.547			62.461, 304.025		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 239 of 264)

Biomarker: Total Nicotine (nmol/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value*	Smokers	Female Non-Smokers	P-value*
Week 1	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	11.833, 10.243	0.015, 0.015		6.930, 6.137	0.029, 0.027	
	SD, SE	6.6791, 3.8562	NA, NA		3.5278, 2.0368	0.0141, 0.0100	
	MEDIAN	13.088	0.015		8.454	0.029	
	MIN, MAX	4.615, 17.795	0.015, 0.015		2.896, 9.439	0.019, 0.039	
	5%, 95%	4.615, 17.795	NA, NA		2.896, 9.439	0.019, 0.039	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1489	3	3	0.0809
	MEAN, GEO MEAN	11.371, 10.429	0.021, 0.020		8.138, 7.501	0.038, 0.037	
	SD, SE	5.8605, 3.3836	0.0071, 0.0050		3.5658, 2.0587	0.0093, 0.0054	
	MEDIAN	9.627	0.021		9.321	0.042	
	MIN, MAX	6.581, 17.906	0.016, 0.026		4.131, 10.962	0.027, 0.044	
	5%, 95%	6.581, 17.906	0.016, 0.026		4.131, 10.962	0.027, 0.044	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.1052	3	3	0.0809
	MEAN, GEO MEAN	8.146, 7.454	0.021, 0.020		8.716, 8.167	0.022, 0.021	
	SD, SE	4.6457, 3.2850	0.0059, 0.0030		4.0438, 2.3347	0.0082, 0.0047	
	MEDIAN	8.146	0.020		6.628	0.024	
	MIN, MAX	4.861, 11.431	0.015, 0.027		6.143, 13.377	0.013, 0.029	
	5%, 95%	4.861, 11.431	0.015, 0.027		6.143, 13.377	0.013, 0.029	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall*	N	3	4	0.0518	3	3	0.0809
	MEAN, GEO MEAN	10.807, 9.848	0.021, 0.020		7.928, 7.381	0.030, 0.030	
	SD, SE	5.2014, 3.0030	0.0061, 0.0031		3.4391, 1.9856	0.0047, 0.0027	
	MEDIAN	11.358	0.021		8.134	0.032	
	MIN, MAX	5.352, 15.711	0.015, 0.027		4.390, 11.259	0.025, 0.034	
	5%, 95%	5.352, 15.711	0.015, 0.027		4.390, 11.259	0.025, 0.034	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (µg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	1	NA	3	2	0.1489
	MEAN, GEO MEAN	1.919, 1.662	0.002, 0.002		1.124, 0.995	0.005, 0.004	
	SD, SE	1.0830, 0.6252	NA, NA		0.5720, 0.3302	0.0021, 0.0015	
	MEDIAN	2.123	0.002		1.371	0.005	
	MIN, MAX	0.749, 2.886	0.002, 0.002		0.470, 1.531	0.003, 0.006	
	5%, 95%	0.749, 2.886	NA, NA		0.470, 1.531	0.003, 0.006	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1489	3	3	0.0765
	MEAN, GEO MEAN	1.844, 1.691	0.004, 0.003		1.320, 1.217	0.006, 0.006	
	SD, SE	0.9506, 0.5489	0.0007, 0.0005		0.5784, 0.3339	0.0017, 0.0010	
	MEDIAN	1.561	0.004		1.512	0.007	
	MIN, MAX	1.067, 2.904	0.003, 0.004		0.670, 1.778	0.004, 0.007	
	5%, 95%	1.067, 2.904	0.003, 0.004		0.670, 1.778	0.004, 0.007	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.1002	3	3	0.0809
	MEAN, GEO MEAN	1.321, 1.209	0.003, 0.003		1.414, 1.324	0.004, 0.003	
	SD, SE	0.7538, 0.5330	0.0010, 0.0005		0.6562, 0.3789	0.0015, 0.0009	
	MEDIAN	1.321	0.004		1.075	0.004	
	MIN, MAX	0.788, 1.854	0.002, 0.004		0.996, 2.170	0.002, 0.005	
	5%, 95%	0.788, 1.854	0.002, 0.004		0.996, 2.170	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0497	3	3	0.0809
	MEAN, GEO MEAN	1.753, 1.597	0.003, 0.003		1.286, 1.197	0.005, 0.005	
	SD, SE	0.8436, 0.4870	0.0010, 0.0005		0.5577, 0.3220	0.0010, 0.0006	
	MEDIAN	1.842	0.004		1.319	0.005	
	MIN, MAX	0.868, 2.548	0.002, 0.004		0.712, 1.826	0.004, 0.006	
	5%, 95%	0.868, 2.548	0.002, 0.004		0.712, 1.826	0.004, 0.006	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 241 of 264)

Biomarker: Total Nicotine ((nmol/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.940, 0.866			0.290, 0.269		
	SD, SE	0.4805, 0.2774			0.1310, 0.0757		
	MEDIAN	0.769			0.286		
	MIN, MAX	0.569, 1.483			0.161, 0.423		
	5%, 95%	0.569, 1.483			0.161, 0.423		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.922, 0.802			0.833, 0.561		
	SD, SE	0.6175, 0.3565			0.8702, 0.5024		
	MEDIAN	0.658			0.466		
	MIN, MAX	0.481, 1.628			0.207, 1.827		
	5%, 95%	0.481, 1.628			0.207, 1.827		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.882, 0.879			0.967, 0.631		
	SD, SE	0.1011, 0.0715			1.0935, 0.6313		
	MEDIAN	0.882			0.341		
	MIN, MAX	0.810, 0.953			0.331, 2.230		
	5%, 95%	0.810, 0.953			0.331, 2.230		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.875, 0.810			0.697, 0.518		
	SD, SE	0.4298, 0.2482			0.6560, 0.3787		
	MEDIAN	0.746			0.407		
	MIN, MAX	0.525, 1.355			0.236, 1.448		
	5%, 95%	0.525, 1.355			0.236, 1.448		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 242 of 264)

Biomarker: Total Nicotine ((µg/mg Creatinine)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.153, 0.140			0.047, 0.044		
	SD, SE	0.0783, 0.0452			0.0215, 0.0124		
	MEDIAN	0.125			0.046		
	MIN, MAX	0.092, 0.241			0.026, 0.069		
	5%, 95%	0.092, 0.241			0.026, 0.069		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.150, 0.130			0.135, 0.091		
	SD, SE	0.1001, 0.0578			0.1407, 0.0812		
	MEDIAN	0.107			0.076		
	MIN, MAX	0.078, 0.264			0.034, 0.296		
	5%, 95%	0.078, 0.264			0.034, 0.296		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.143, 0.142			0.157, 0.102		
	SD, SE	0.0170, 0.0120			0.1775, 0.1025		
	MEDIAN	0.143			0.055		
	MIN, MAX	0.131, 0.155			0.054, 0.362		
	5%, 95%	0.131, 0.155			0.054, 0.362		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.142, 0.131			0.113, 0.084		
	SD, SE	0.0699, 0.0404			0.1066, 0.0615		
	MEDIAN	0.121			0.066		
	MIN, MAX	0.085, 0.220			0.038, 0.235		
	5%, 95%	0.085, 0.220			0.038, 0.235		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (nmol/L) Analytical Lab: INBIFO		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	1	NA	3	2	0.1386
	MEAN, GEO MEAN	15881.3, 12002.3	12.7, 12.7		3716.4, 3522.0	12.7, 12.7	
	SD, SE	12560.28, 7251.68	NA, NA		1519.43, 877.25	0.00, 0.00	
	MEDIAN	14410.2	12.7		3272.1	12.7	
	MIN, MAX	4121.4, 29112.4	12.7, 12.7		2468.7, 5408.5	12.7, 12.7	
	5%, 95%	4121.4, 29112.4	NA, NA		2468.7, 5408.5	12.7, 12.7	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1386	3	3	0.0765
	MEAN, GEO MEAN	13046.6, 10206.2	12.7, 12.7		4821.8, 4348.3	24.9, 20.0	
	SD, SE	9005.77, 5199.48	0.00, 0.00		2813.16, 1624.18	21.19, 12.23	
	MEDIAN	14296.8	12.7		3453.4	12.7	
	MIN, MAX	3481.1, 21362.0	12.7, 12.7		2954.7, 8057.4	12.7, 49.4	
	5%, 95%	3481.1, 21362.0	12.7, 12.7		2954.7, 8057.4	12.7, 49.4	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.0532	3	3	0.0636
	MEAN, GEO MEAN	5553.6, 4245.8	12.7, 12.7		5049.5, 4741.8	12.7, 12.7	
	SD, SE	5062.67, 3579.85	0.00, 0.00		1969.90, 1137.32	0.00, 0.00	
	MEDIAN	5553.6	12.7		5824.0	12.7	
	MIN, MAX	1973.7, 9133.4	12.7, 12.7		2810.1, 6514.5	12.7, 12.7	
	5%, 95%	1973.7, 9133.4	12.7, 12.7		2810.1, 6514.5	12.7, 12.7	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall ^b	N	3	4	0.0319	3	3	0.0765
	MEAN, GEO MEAN	12471.6, 9691.8	12.7, 12.7		4529.3, 4244.4	16.8, 15.9	
	SD, SE	8496.37, 4905.38	0.00, 0.00		1980.61, 1143.50	7.04, 4.07	
	MEDIAN	14353.5	12.7		4183.2	12.7	
	MIN, MAX	3192.1, 19869.3	12.7, 12.7		2744.5, 6660.1	12.7, 24.9	
	5%, 95%	3192.1, 19869.3	12.7, 12.7		2744.5, 6660.1	12.7, 24.9	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Total Nicotine (ng/mL) Analytical Lab: INBIFO		Male			Female		
Timepoint	Statistic	Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	3	1	NA	3	2	0.1386
	MEAN, GEO MEAN	2575.9, 1946.8	2.1, 2.1		602.8, 571.3	2.1, 2.1	
	SD, SE	2037.26, 1176.21	NA, NA		246.49, 142.31	0.00, 0.00	
	MEDIAN	2337.3	2.1		530.7	2.1	
	MIN, MAX	668.5, 4722.0	2.1, 2.1		400.4, 877.3	2.1, 2.1	
	5%, 95%	668.5, 4722.0	NA, NA		400.4, 877.3	2.1, 2.1	
	# of BLQ/ALQ Values	0/0	1/0		0/0	2/0	
Week 2	N	3	2	0.1386	3	3	0.0765
	MEAN, GEO MEAN	2116.1, 1655.4	2.1, 2.1		782.1, 705.3	4.1, 3.3	
	SD, SE	1460.74, 843.36	0.00, 0.00		456.28, 263.43	3.41, 1.97	
	MEDIAN	2318.9	2.1		560.1	2.1	
	MIN, MAX	564.6, 3464.9	2.1, 2.1		479.3, 1306.9	2.1, 8.0	
	5%, 95%	564.6, 3464.9	2.1, 2.1		479.3, 1306.9	2.1, 8.0	
	# of BLQ/ALQ Values	0/0	2/0		0/0	2/0	
Week 3	N	2	4	0.0552	3	3	0.0636
	MEAN, GEO MEAN	900.8, 688.6	2.1, 2.1		819.1, 769.1	2.1, 2.1	
	SD, SE	821.16, 580.65	0.00, 0.00		319.54, 184.49	0.00, 0.00	
	MEDIAN	900.8	2.1		944.7	2.1	
	MIN, MAX	320.1, 1481.4	2.1, 2.1		455.8, 1056.7	2.1, 2.1	
	5%, 95%	320.1, 1481.4	2.1, 2.1		455.8, 1056.7	2.1, 2.1	
	# of BLQ/ALQ Values	0/0	4/0		0/0	3/0	
Overall*	N	3	4	0.0319	3	3	0.0765
	MEAN, GEO MEAN	2022.9, 1571.9	2.1, 2.1		734.7, 688.5	2.8, 2.6	
	SD, SE	1378.14, 795.67	0.00, 0.00		321.25, 185.48	1.15, 0.67	
	MEDIAN	2328.1	2.1		678.5	2.1	
	MIN, MAX	517.7, 3222.8	2.1, 2.1		445.2, 1080.3	2.1, 4.1	
	5%, 95%	517.7, 3222.8	2.1, 2.1		445.2, 1080.3	2.1, 4.1	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439412

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 245 of 264)

Biomarker: Total Nicotine ((nmol/L)/cigarette per day)		Analytical Lab: INBJFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1246.5, 1014.5			156.4, 154.3		
	SD, SE	1021.95, 590.02			29.92, 17.27		
	MEDIAN	686.9			163.9		
	MIN, MAX	626.5, 2426.0			123.4, 181.8		
	5%, 95%	626.5, 2426.0			123.4, 181.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1001.6, 784.7			554.4, 324.8		
	SD, SE	834.77, 481.95			682.95, 394.30		
	MEDIAN	714.8			172.7		
	MIN, MAX	348.1, 1942.0			147.7, 1342.9		
	5%, 95%	348.1, 1942.0			147.7, 1342.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	545.1, 500.4			516.6, 366.8		
	SD, SE	305.54, 216.05			501.34, 289.45		
	MEDIAN	545.1			323.6		
	MIN, MAX	329.0, 761.1			140.5, 1085.8		
	5%, 95%	329.0, 761.1			140.5, 1085.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	945.0, 804.9			409.1, 299.2		
	SD, SE	670.97, 387.38			396.59, 228.97		
	MEDIAN	670.7			226.0		
	MIN, MAX	454.7, 1709.7			137.2, 864.2		
	5%, 95%	454.7, 1709.7			137.2, 864.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439413

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 246 of 264)

Biomarker: Total Nicotine ((ng/mL)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	202.2, 164.5			25.4, 25.0		
	SD, SE	165.77, 95.71			4.87, 2.81		
	MEDIAN	111.4			26.6		
	MIN, MAX	101.6, 393.5			20.0, 29.5		
	5%, 95%	101.6, 393.5			20.0, 29.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	162.5, 127.3			89.9, 52.7		
	SD, SE	135.40, 78.17			110.75, 63.94		
	MEDIAN	115.9			28.0		
	MIN, MAX	56.5, 315.0			24.0, 217.8		
	5%, 95%	56.5, 315.0			24.0, 217.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	88.5, 81.2			83.8, 59.5		
	SD, SE	49.57, 35.05			81.30, 46.94		
	MEDIAN	88.5			52.5		
	MIN, MAX	53.4, 123.5			22.8, 176.1		
	5%, 95%	53.4, 123.5			22.8, 176.1		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	153.3, 130.6			66.4, 48.6		
	SD, SE	108.80, 62.82			64.32, 37.13		
	MEDIAN	108.8			36.7		
	MIN, MAX	73.8, 277.3			22.3, 140.2		
	5%, 95%	73.8, 277.3			22.3, 140.2		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

PM3006439414

RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 247 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/24hr) Analytical Lab: INBIFO

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	21069.866, 18521.314	23.647, 19.239		33503.660, 32205.856	31.839, 22.520	
	SD, SE	12742.2766, 7356.7568	16.1872, 8.0936		12057.0021, 6961.1134	24.8055, 12.4027	
	MEDIAN	18354.825	21.714		27146.280	32.462	
	MIN, MAX	9903.928, 34950.846	8.732, 42.427		25955.790, 47408.910	5.880, 56.550	
	5%, 95%	9903.928, 34950.846	8.732, 42.427		25955.790, 47408.910	5.880, 56.550	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0518
	MEAN, GEO MEAN	18485.545, 16208.505	35.046, 28.936		39075.955, 34277.605	20.636, 19.147	
	SD, SE	11611.4462, 6703.8716	20.9069, 12.0706		25209.8818, 14554.9320	8.8182, 4.4091	
	MEDIAN	14936.916	46.368		28809.570	20.185	
	MIN, MAX	9062.489, 31457.230	10.920, 47.850		20619.126, 67799.170	10.712, 31.460	
	5%, 95%	9062.489, 31457.230	10.920, 47.850		20619.126, 67799.170	10.712, 31.460	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	12276.934, 10259.210	25.412, 22.925		26289.321, 21251.072	19.817, 17.623	
	SD, SE	9536.4260, 6743.2715	15.5047, 10.9635		21905.9976, 12647.4336	11.2455, 6.4926	
	MEDIAN	12276.934	25.412		13910.514	18.228	
	MIN, MAX	5533.662, 19020.205	14.448, 36.375		13375.150, 51582.300	9.450, 31.772	
	5%, 95%	5533.662, 19020.205	14.448, 36.375		13375.150, 51582.300	9.450, 31.772	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	19602.682, 16784.391	23.274, 19.026		32956.312, 29610.296	23.819, 20.460	
	SD, SE	12658.3479, 7308.3006	15.4570, 7.7285		19636.8122, 11337.3188	13.4686, 6.7343	
	MEDIAN	17437.315	22.844		22713.503	24.725	
	MIN, MAX	8166.693, 33204.038	8.732, 38.675		20558.640, 55596.793	8.681, 37.147	
	5%, 95%	8166.693, 33204.038	8.732, 38.675		20558.640, 55596.793	8.681, 37.147	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 248 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	4049.628, 3559.797	4,545, 3,697		6439.404, 6189.966	6,119, 4,328	
	SD, SE	2449.0658, 1413.9688	3,111.1, 1,555.5		2317.3560, 1337.9261	4,767.7, 2,383.8	
	MEDIAN	3527.797	4,174		5217.515	6,239	
	MIN, MAX	1903.535, 6717.553	1,678, 8,154		4988.703, 9111.993	1,130, 10,869	
	5%, 95%	1903.535, 6717.553	1,678, 8,154		4988.703, 9111.993	1,130, 10,869	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0518
	MEAN, GEO MEAN	3552.922, 3115.274	6,736, 5,562		7510.398, 6588.155	3,966, 3,680	
	SD, SE	2231.7204, 1288.4844	4,018.3, 2,320.0		4845.3391, 2797.4578	1,695.0, 0.8475	
	MEDIAN	2870.875	8,912		5537.199	3,880	
	MIN, MAX	1741.810, 6046.080	2,099, 9,197		3962.996, 13031.000	2,059, 6,047	
	5%, 95%	1741.810, 6046.080	2,099, 9,197		3962.996, 13031.000	2,059, 6,047	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	2359.627, 1971.820	4,884, 4,406		5052.808, 4084.456	3,809, 3,387	
	SD, SE	1832.9007, 1296.0565	2,979.7, 2,107.0		4210.3326, 2430.8367	2,161.8, 1,248.1	
	MEDIAN	2359.627	4,884		2673.601	3,503	
	MIN, MAX	1063.570, 3655.683	2,777, 6,991		2570.704, 9914.118	1,816, 6,107	
	5%, 95%	1063.570, 3655.683	2,777, 6,991		2570.704, 9914.118	1,816, 6,107	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall*	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	3767.636, 3225.960	4,473, 3,657		6334.203, 5691.099	4,578, 3,932	
	SD, SE	2432.9351, 1404.6557	2,970.7, 1,485.3		3774.1955, 2179.0328	2,589.1, 1,294.6	
	MEDIAN	3351.452	4,391		4365.535	4,752	
	MIN, MAX	1569.638, 6381.817	1,678, 7,433		3951.371, 10685.704	1,668, 7,140	
	5%, 95%	1569.638, 6381.817	1,678, 7,433		3951.371, 10685.704	1,668, 7,140	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 249 of 264)

Biomarker: Trans-3-hydroxyxanthine ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1566.609, 1563.493			1555.037, 1411.441		
	SD, SE	72.9567, 42.1215			792.9948, 457.8358		
	MEDIAN	1529.569			1508.127		
	MIN, MAX	1519.602, 1650.655			786.539, 2370.446		
	5%, 95%	1519.602, 1650.655			786.539, 2370.446		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1279.004, 1246.241			3074.170, 2560.197		
	SD, SE	340.2378, 196.4364			1905.0516, 1099.8821		
	MEDIAN	1357.901			3389.959		
	MIN, MAX	906.249, 1572.862			1030.956, 4801.595		
	5%, 95%	906.249, 1572.862			1030.956, 4801.595		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1253.647, 1209.059			1860.371, 1643.979		
	SD, SE	468.6279, 331.3700			957.9717, 553.0852		
	MEDIAN	1253.647			2229.192		
	MIN, MAX	922.277, 1585.017			772.806, 2579.115		
	5%, 95%	922.277, 1585.017			772.806, 2579.115		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1398.929, 1387.883			2163.193, 1999.726		
	SD, SE	208.9993, 120.6658			921.4392, 531.9932		
	MEDIAN	1490.829			2605.775		
	MIN, MAX	1159.727, 1546.232			1103.963, 2779.840		
	5%, 95%	1159.727, 1546.232			1103.963, 2779.840		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 250 of 264)

Biomarker: Trans-3-hydroxycotinine ((pg/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	301.102, 300.888			298.878, 271.279		
	SD, SE	14.0222, 8.0957			152.4136, 87.9961		
	MEDIAN	293.983			289.862		
	MIN, MAX	292.068, 317.256			151.173, 455.600		
	5%, 95%	292.068, 317.256			151.173, 455.600		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	245.825, 239.528			590.856, 492.070		
	SD, SE	65.3938, 37.7551			366.1510, 211.3974		
	MEDIAN	260.989			651.550		
	MIN, MAX	174.181, 302.304			198.150, 922.867		
	5%, 95%	174.181, 302.304			198.150, 922.867		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	240.951, 232.381			357.563, 315.973		
	SD, SE	90.0698, 63.6890			184.1224, 106.3031		
	MEDIAN	240.951			428.451		
	MIN, MAX	177.262, 304.640			148.533, 495.706		
	5%, 95%	177.262, 304.640			148.533, 495.706		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	268.874, 266.751			415.766, 384.347		
	SD, SE	40.1694, 23.1918			177.1004, 102.2489		
	MEDIAN	286.537			500.830		
	MIN, MAX	222.900, 297.186			212.182, 534.285		
	5%, 95%	222.900, 297.186			212.182, 534.285		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 251 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine) Analytical Lab: INBIFO

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	13.589, 12.752	0.011, 0.010		29.592, 24.553	0.024, 0.019	
	SD, SE	5.8121, 3.3556	0.0055, 0.0027		22.9539, 13.2525	0.0157, 0.0079	
	MEDIAN	12.896	0.011		18.489	0.024	
	MIN, MAX	8.155, 19.717	0.005, 0.018		14.300, 55.986	0.007, 0.041	
	5%, 95%	8.155, 19.717	0.005, 0.018		14.300, 55.986	0.007, 0.041	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0518
	MEAN, GEO MEAN	14.498, 13.787	0.015, 0.014		33.227, 25.023	0.017, 0.016	
	SD, SE	5.6224, 3.2461	0.0067, 0.0038		31.1085, 17.9605	0.0074, 0.0037	
	MEDIAN	13.463	0.017		18.231	0.018	
	MIN, MAX	9.465, 20.566	0.008, 0.021		12.457, 68.993	0.009, 0.024	
	5%, 95%	9.465, 20.566	0.008, 0.021		12.457, 68.993	0.009, 0.024	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	12.618, 12.316	0.012, 0.011		23.925, 18.098	0.022, 0.019	
	SD, SE	3.8757, 2.7405	0.0057, 0.0040		22.3492, 12.9033	0.0125, 0.0072	
	MEDIAN	12.618	0.012		12.774	0.026	
	MIN, MAX	9.877, 15.358	0.008, 0.016		9.346, 49.656	0.008, 0.032	
	5%, 95%	9.877, 15.358	0.008, 0.016		9.346, 49.656	0.008, 0.032	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^a	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	14.405, 13.693	0.011, 0.010		28.915, 22.609	0.020, 0.018	
	SD, SE	5.5050, 3.1783	0.0050, 0.0025		25.4702, 14.7052	0.0111, 0.0056	
	MEDIAN	13.906	0.012		16.498	0.021	
	MIN, MAX	9.166, 20.142	0.005, 0.016		12.034, 58.212	0.008, 0.032	
	5%, 95%	9.166, 20.142	0.005, 0.016		12.034, 58.212	0.008, 0.032	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

^a P-value from Wilcoxon rank-sum test.

^a Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 252 of 264)

Biomarker: Trans-3-hydroxycotinine (µg/mg Creatinine)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0497	3	4	0.0518
	MEAN, GEO MEAN	2.612, 2.451	0.002, 0.002		5.688, 4.719	0.005, 0.003	
	SD, SE	1.1175, 0.6452	0.0008, 0.0004		4.4121, 2.5473	0.0031, 0.0016	
	MEDIAN	2.479	0.002		3.554	0.005	
	MIN, MAX	1.567, 3.790	0.001, 0.003		2.748, 10.761	0.001, 0.008	
	5%, 95%	1.567, 3.790	0.001, 0.003		2.748, 10.761	0.001, 0.008	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0497
	MEAN, GEO MEAN	2.787, 2.650	0.003, 0.003		6.386, 4.809	0.003, 0.003	
	SD, SE	1.0808, 0.6240	0.0010, 0.0006		5.9789, 3.4519	0.0015, 0.0008	
	MEDIAN	2.588	0.003		3.504	0.003	
	MIN, MAX	1.819, 3.953	0.002, 0.004		2.394, 13.260	0.002, 0.005	
	5%, 95%	1.819, 3.953	0.002, 0.004		2.394, 13.260	0.002, 0.005	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	2.425, 2.367	0.003, 0.002		4.598, 3.478	0.004, 0.004	
	SD, SE	0.7453, 0.5270	0.0007, 0.0005		4.2957, 2.4801	0.0021, 0.0012	
	MEDIAN	2.425	0.003		2.455	0.005	
	MIN, MAX	1.898, 2.952	0.002, 0.003		1.796, 9.544	0.002, 0.006	
	5%, 95%	1.898, 2.952	0.002, 0.003		1.796, 9.544	0.002, 0.006	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall*	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	2.769, 2.632	0.002, 0.002		5.557, 4.346	0.004, 0.004	
	SD, SE	1.0587, 0.6113	0.0010, 0.0005		4.8951, 2.8262	0.0018, 0.0009	
	MEDIAN	2.673	0.003		3.171	0.004	
	MIN, MAX	1.761, 3.872	0.001, 0.003		2.313, 11.188	0.002, 0.006	
	5%, 95%	1.761, 3.872	0.001, 0.003		2.313, 11.188	0.002, 0.006	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 253 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/mg Creatinine)/cigarette per day		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	1.097, 1.078			1.384, 1.076		
	SD, SE	0.2517, 0.1453			1.2307, 0.7106		
	MEDIAN	1.075			0.794		
	MIN, MAX	0.857, 1.359			0.560, 2.799		
	5%, 95%	0.857, 1.359			0.560, 2.799		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	1.066, 1.060			2.371, 1.869		
	SD, SE	0.1424, 0.0822			1.5274, 0.8819		
	MEDIAN	1.028			3.039		
	MIN, MAX	0.947, 1.224			0.623, 3.450		
	5%, 95%	0.947, 1.224			0.623, 3.450		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1.463, 1.452			1.710, 1.400		
	SD, SE	0.2588, 0.1830			1.0468, 0.6044		
	MEDIAN	1.463			2.129		
	MIN, MAX	1.280, 1.646			0.519, 2.483		
	5%, 95%	1.280, 1.646			0.519, 2.483		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	1.151, 1.140			1.822, 1.530		
	SD, SE	0.1905, 0.1100			1.1355, 0.6556		
	MEDIAN	1.193			1.909		
	MIN, MAX	0.943, 1.317			0.645, 2.911		
	5%, 95%	0.943, 1.317			0.645, 2.911		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 254 of 264)

Biomarker: Trans-3-hydroxycotinine ((µg/mg Creatinine)/cigarette per day) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.211, 0.207			0.266, 0.207		
	SD, SE	0.0481, 0.0278			0.2363, 0.1365		
	MEDIAN	0.207			0.153		
	MIN, MAX	0.165, 0.261			0.108, 0.538		
	5%, 95%	0.165, 0.261			0.108, 0.538		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.205, 0.204			0.456, 0.360		
	SD, SE	0.0272, 0.0157			0.2934, 0.1694		
	MEDIAN	0.198			0.584		
	MIN, MAX	0.182, 0.235			0.120, 0.663		
	5%, 95%	0.182, 0.235			0.120, 0.663		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.281, 0.279			0.329, 0.269		
	SD, SE	0.0495, 0.0350			0.2009, 0.1160		
	MEDIAN	0.281			0.409		
	MIN, MAX	0.246, 0.316			0.100, 0.477		
	5%, 95%	0.246, 0.316			0.100, 0.477		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.221, 0.219			0.350, 0.294		
	SD, SE	0.0361, 0.0209			0.2180, 0.1259		
	MEDIAN	0.229			0.367		
	MIN, MAX	0.182, 0.253			0.124, 0.559		
	5%, 95%	0.182, 0.253			0.124, 0.559		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 255 of 264)

Biomarker: Trans-3-hydroxycotinine (nmol/L)		Analytical Lab: INBIFO					
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	3	4	0.0518	3	4	0.0497
	MEAN, GEO MEAN	16696.1, 14940.9	13.5, 10.3		14366.9, 14092.1	12.2, 9.7	
	SD, SE	8158.34, 4710.22	12.46, 6.23		3268.60, 1887.13	8.60, 4.30	
	MEDIAN	21097.5	8.3		16158.5	11.2	
	MIN, MAX	7282.3, 21708.6	5.7, 31.9		10594.2, 16347.9	4.9, 21.6	
	5%, 95%	7282.3, 21708.6	5.7, 31.9		10594.2, 16347.9	4.9, 21.6	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0518
	MEAN, GEO MEAN	17203.0, 13492.0	17.2, 14.6		15228.1, 14505.1	9.4, 8.8	
	SD, SE	12805.29, 7393.14	10.55, 6.09		5943.28, 3431.36	3.79, 1.90	
	MEDIAN	16061.2	17.4		13399.8	8.6	
	MIN, MAX	5006.9, 30541.0	6.5, 27.6		10413.7, 21870.7	6.0, 14.3	
	5%, 95%	5006.9, 30541.0	6.5, 27.6		10413.7, 21870.7	6.0, 14.3	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	8140.5, 7014.7	9.8, 9.4		12045.1, 10508.6	12.3, 11.6	
	SD, SE	5841.55, 4130.60	3.89, 2.75		7912.77, 4568.44	4.70, 2.71	
	MEDIAN	8140.5	9.8		8860.2	12.4	
	MIN, MAX	4009.9, 12271.1	7.0, 12.5		6221.0, 21054.0	7.5, 16.9	
	5%, 95%	4009.9, 12271.1	7.0, 12.5		6221.0, 21054.0	7.5, 16.9	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	16011.5, 13273.5	11.9, 10.2		13880.0, 13295.5	10.7, 9.8	
	SD, SE	10353.74, 5977.73	7.71, 3.85		5163.80, 2981.32	4.99, 2.50	
	MEDIAN	16476.6	9.8		11810.8	10.7	
	MIN, MAX	5433.0, 26124.8	5.9, 22.2		10071.7, 19757.5	5.5, 16.1	
	5%, 95%	5433.0, 26124.8	5.9, 22.2		10071.7, 19757.5	5.5, 16.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 256 of 264)

Biomarker: Trans-3-hydroxycotinine (ng/mL)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	4	0.0497	3	4	0.0497
	MEAN, GEO MEAN	3209.0, 2871.7	2.6, 2.0		2761.3, 2708.5	2.3, 1.8	
	SD, SE	1568.00, 905.29	2.39, 1.19		628.25, 362.72	1.69, 0.84	
	MEDIAN	4054.9	1.6		3105.7	2.1	
	MIN, MAX	1399.7, 4172.4	1.1, 6.1		2036.2, 3142.1	0.9, 4.2	
	5%, 95%	1399.7, 4172.4	1.1, 6.1		2036.2, 3142.1	0.9, 4.2	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	3	0.0809	3	4	0.0518
	MEAN, GEO MEAN	3306.4, 2593.2	3.3, 2.8		2926.8, 2787.9	1.8, 1.7	
	SD, SE	2461.20, 1420.97	2.05, 1.18		1142.28, 659.50	0.70, 0.35	
	MEDIAN	3087.0	3.3		2575.4	1.7	
	MIN, MAX	962.3, 5870.0	1.2, 5.3		2001.5, 4203.5	1.2, 2.7	
	5%, 95%	962.3, 5870.0	1.2, 5.3		2001.5, 4203.5	1.2, 2.7	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	2	2	0.2453	3	3	0.0809
	MEAN, GEO MEAN	1564.6, 1348.2	1.9, 1.8		2315.1, 2019.8	2.3, 2.2	
	SD, SE	1122.74, 793.90	0.78, 0.55		1520.84, 878.06	0.90, 0.52	
	MEDIAN	1564.6	1.9		1702.9	2.4	
	MIN, MAX	770.7, 2358.5	1.3, 2.4		1195.7, 4046.6	1.4, 3.2	
	5%, 95%	770.7, 2358.5	1.3, 2.4		1195.7, 4046.6	1.4, 3.2	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	3	4	0.0518	3	4	0.0518
	MEAN, GEO MEAN	3077.4, 2551.2	2.3, 1.9		2667.7, 2555.4	2.1, 1.9	
	SD, SE	1990.01, 1148.93	1.45, 0.73		992.49, 573.01	0.95, 0.48	
	MEDIAN	3166.8	1.9		2270.0	2.0	
	MIN, MAX	1044.2, 5021.2	1.1, 4.2		1935.8, 3797.4	1.1, 3.1	
	5%, 95%	1044.2, 5021.2	1.1, 4.2		1935.8, 3797.4	1.1, 3.1	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 257 of 264)

Biomarker: Trans-3-hydroxycotinine ((nmol/L)/cigarette per day)		Analytical Lab: INBIFO				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	1305.2, 1262.9			678.7, 617.6	
	SD, SE	414.75, 239.45			312.37, 180.35	
	MEDIAN	1213.7			817.4	
	MIN, MAX	943.9, 1758.1			321.0, 897.7	
	5%, 95%	943.9, 1758.1			321.0, 897.7	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	1162.6, 1037.4			1282.5, 1083.4	
	SD, SE	574.23, 331.53			871.80, 503.34	
	MEDIAN	1460.1			1093.5	
	MIN, MAX	500.7, 1527.1			520.7, 2233.3	
	5%, 95%	500.7, 1527.1			520.7, 2233.3	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	845.5, 826.7			860.6, 812.9	
	SD, SE	250.53, 177.15			319.11, 184.24	
	MEDIAN	845.5			1036.8	
	MIN, MAX	668.3, 1022.6			492.2, 1052.7	
	5%, 95%	668.3, 1022.6			492.2, 1052.7	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	1147.8, 1115.2			940.6, 909.8	
	SD, SE	318.88, 184.11			283.03, 163.41	
	MEDIAN	1235.5			987.9	
	MIN, MAX	794.2, 1413.6			636.9, 1197.0	
	5%, 95%	794.2, 1413.6			636.9, 1197.0	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 258 of 264)

Biomarker: Trans-3-hydroxycotinine ((ng/mL/cigarette per day)		Analytical Lab: INB/FO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	250.9, 242.7			130.4, 118.7		
	SD, SE	79.72, 46.02			60.02, 34.65		
	MEDIAN	233.3			157.1		
	MIN, MAX	181.4, 337.9			61.7, 172.5		
	5%, 95%	181.4, 337.9			61.7, 172.5		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	223.4, 199.4			246.5, 208.2		
	SD, SE	110.38, 63.73			167.53, 96.72		
	MEDIAN	280.6			210.2		
	MIN, MAX	96.2, 293.5			100.1, 429.2		
	5%, 95%	96.2, 293.5			100.1, 429.2		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	162.5, 158.9			165.4, 156.2		
	SD, SE	48.08, 34.00			61.33, 35.41		
	MEDIAN	162.5			199.3		
	MIN, MAX	128.5, 196.5			94.6, 202.3		
	5%, 95%	128.5, 196.5			94.6, 202.3		
	# of BLQ/ALQ Values	0/0			0/0		
Overall [*]	N	3		NA	3		NA
	MEAN, GEO MEAN	220.6, 214.4			180.8, 174.9		
	SD, SE	61.27, 35.37			54.42, 31.42		
	MEDIAN	237.5			189.9		
	MIN, MAX	152.7, 271.7			122.4, 230.1		
	5%, 95%	152.7, 271.7			122.4, 230.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^{*} Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 259 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/L) Analytical Lab: INBIFO

Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	2967.6, 2577.2	12.6, 12.6		3491.0, 3364.4	23.5, 23.5	
	SD, SE	1587.37, 916.47	NA, NA		1069.44, 617.44	NA, NA	
	MEDIAN	3869.9	12.6		4093.9	23.5	
	MIN, MAX	1134.7, 3898.1	12.6, 12.6		2256.2, 4122.8	23.5, 23.5	
	5%, 95%	1134.7, 3898.1	NA, NA		2256.2, 4122.8	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	1	NA	3		NA
	MEAN, GEO MEAN	5047.3, 4630.8	14.3, 14.3		2475.6, 2404.6		
	SD, SE	2322.19, 1340.72	NA, NA		758.18, 437.73		
	MEDIAN	5439.6	14.3		2146.2		
	MIN, MAX	2553.9, 7148.3	14.3, 14.3		1937.9, 3342.8		
	5%, 95%	2553.9, 7148.3	NA, NA		1937.9, 3342.8		
	# of BLQ/ALQ Values	0/0	0/0		0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	1746.4, 932.8			2906.2, 1703.6		
	SD, SE	2087.94, 1476.40			3474.95, 2006.26		
	MEDIAN	1746.4			1240.5		
	MIN, MAX	270.0, 3222.8			577.6, 6900.4		
	5%, 95%	270.0, 3222.8			577.6, 6900.4		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	3671.8, 3122.2	13.5, 13.5		2957.6, 2709.5	23.5, 23.5	
	SD, SE	2141.75, 1236.54	NA, NA		1586.08, 915.72	NA, NA	
	MEDIAN	4186.8	13.5		2212.8	23.5	
	MIN, MAX	1319.5, 5509.1	13.5, 13.5		1881.0, 4779.0	23.5, 23.5	
	5%, 95%	1319.5, 5509.1	NA, NA		1881.0, 4779.0	NA, NA	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Covance CRU Study No. 12226-8450

Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 260 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/L/cigarette per day)		Analytical Lab: (NB)FO				
Timepoint	Statistic	Male		P-value ^a	Female	
		Smokers	Non-Smokers		Smokers	Non-Smokers
Week 1	N	3		NA	3	NA
	MEAN, GEO MEAN	227.4, 217.8			167.4, 147.5	
	SD, SE	84.99, 49.07			86.56, 49.98	
	MEDIAN	189.1			204.7	
	MIN, MAX	168.3, 324.8			68.4, 229.0	
	5%, 95%	168.3, 324.8			68.4, 229.0	
	# of BLQ/ALQ Values	0/0			0/0	
Week 2	N	3		NA	3	NA
	MEAN, GEO MEAN	369.1, 356.1			207.2, 179.6	
	SD, SE	119.98, 69.27			134.95, 77.91	
	MEDIAN	357.4			167.1	
	MIN, MAX	255.4, 494.5			96.9, 357.7	
	5%, 95%	255.4, 494.5			96.9, 357.7	
	# of BLQ/ALQ Values	0/0			0/0	
Week 3	N	2		NA	3	NA
	MEAN, GEO MEAN	156.8, 109.9			194.6, 131.8	
	SD, SE	158.11, 111.80			156.80, 90.53	
	MEDIAN	156.8			206.8	
	MIN, MAX	45.0, 268.6			32.1, 345.0	
	5%, 95%	45.0, 268.6			32.1, 345.0	
	# of BLQ/ALQ Values	0/0			0/0	
Overall ^b	N	3		NA	3	NA
	MEAN, GEO MEAN	262.9, 249.6			189.7, 181.8	
	SD, SE	99.70, 57.56			62.57, 36.13	
	MEDIAN	262.9			211.0	
	MIN, MAX	163.2, 362.6			119.3, 238.9	
	5%, 95%	163.2, 362.6			119.3, 238.9	

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 261 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/24hr)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	3721.693, 3194.768	16.758, 16.758		8108.768, 7688.828	76.375, 76.375	
	SD, SE	2361.0700, 1363.1644	NA, NA		3333.4991, 1924.5966	NA, NA	
	MEDIAN	3391.347	16.758		6926.304	76.375	
	MIN, MAX	1543.192, 6230.539	16.758, 16.758		5527.690, 11872.310	76.375, 76.375	
	5%, 95%	1543.192, 6230.539	NA, NA		5527.690, 11872.310	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	1	NA	3		NA
	MEAN, GEO MEAN	5681.379, 5563.193	24.024, 24.024		6271.351, 5682.321		
	SD, SE	1472.3577, 850.0661	NA, NA		3564.4461, 2057.9339		
	MEDIAN	5058.828	24.024		4614.330		
	MIN, MAX	4622.559, 7362.749	24.024, 24.024		3837.042, 10362.680		
	5%, 95%	4622.559, 7362.749	NA, NA		3837.042, 10362.680		
	# of BLQ/ALQ Values	0/0	0/0		0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	2683.970, 1364.281			6826.629, 3445.092		
	SD, SE	3268.7708, 2311.3700			8773.2321, 5065.2279		
	MEDIAN	2683.970			2667.075		
	MIN, MAX	372.600, 4995.340			906.832, 16905.980		
	5%, 95%	372.600, 4995.340			906.832, 16905.980		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	4485.977, 4049.169	20.391, 20.391		7068.916, 6006.496	76.375, 76.375	
	SD, SE	2308.5998, 1332.8707	NA, NA		5180.6429, 2991.0456	NA, NA	
	MEDIAN	4481.838	20.391		4269.698	76.375	
	MIN, MAX	2179.450, 6796.644	20.391, 20.391		3890.059, 13046.990	76.375, 76.375	
	5%, 95%	2179.450, 6796.644	NA, NA		3890.059, 13046.990	NA, NA	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 262 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/24hr)/cigarette per day)		Analytical Lab: INBIFO					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	270.235, 270.034			381.972, 336.968		
	SD, SE	12.7193, 7.3435			213.0690, 123.0155		
	MEDIAN	270.893			384.795		
	MIN, MAX	257.199, 282.612			167.506, 593.616		
	5%, 95%	257.199, 282.612			167.506, 593.616		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	430.095, 427.743			493.014, 424.413		
	SD, SE	53.6705, 30.9867			289.4203, 167.0969		
	MEDIAN	459.893			518.134		
	MIN, MAX	368.137, 462.256			191.852, 769.055		
	5%, 95%	368.137, 462.256			191.852, 769.055		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	239.189, 160.782			446.731, 266.513		
	SD, SE	250.4417, 177.0890			397.4641, 229.4760		
	MEDIAN	239.189			444.513		
	MIN, MAX	62.100, 416.278			50.380, 845.299		
	5%, 95%	62.100, 416.278			50.380, 845.299		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	322.098, 317.983			440.572, 397.418		
	SD, SE	62.9113, 36.3218			222.3318, 128.3633		
	MEDIAN	319.515			460.358		
	MIN, MAX	260.518, 386.261			209.009, 652.350		
	5%, 95%	260.518, 386.261			209.009, 652.350		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234* will be used as 1.234*) for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
(Page 263 of 264)

Biomarker: Trans-3-hydroxycotinine-O-glucuronide (nmol/mg Creatinine) Analytical Lab: INBIFO

Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	2.390, 2.200	0.007, 0.007		7.202, 5.862	0.055, 0.055	
	SD, SE	1.1220, 0.6478	NA, NA		5.9063, 3.4100	NA, NA	
	MEDIAN	2.383	0.007		3.938	0.055	
	MIN, MAX	1.271, 3.515	0.007, 0.007		3.648, 14.020	0.055, 0.055	
	5%, 95%	1.271, 3.515	NA, NA		3.648, 14.020	NA, NA	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	3	1	NA	3		NA
	MEAN, GEO MEAN	4.734, 4.732	0.009, 0.009		5.261, 4.148		
	SD, SE	0.1509, 0.0871	NA, NA		4.5860, 2.6477		
	MEDIAN	4.814	0.009		2.920		
	MIN, MAX	4.560, 4.828	0.009, 0.009		2.318, 10.545		
	5%, 95%	4.560, 4.828	NA, NA		2.318, 10.545		
	# of BLQ/ALQ Values	0/0	0/0		0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	2.350, 1.638			6.477, 2.934		
	SD, SE	2.3822, 1.6845			8.5405, 4.9308		
	MEDIAN	2.350			2.547		
	MIN, MAX	0.665, 4.034			0.609, 16.275		
	5%, 95%	0.665, 4.034			0.609, 16.275		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3	1	NA	3	1	NA
	MEAN, GEO MEAN	3.360, 3.251	0.008, 0.008		6.313, 4.540	0.055, 0.055	
	SD, SE	0.9896, 0.5713	NA, NA		6.3393, 3.6600	NA, NA	
	MEDIAN	3.659	0.008		3.135	0.055	
	MIN, MAX	2.255, 4.165	0.008, 0.008		2.192, 13.613	0.055, 0.055	
	5%, 95%	2.255, 4.165	NA, NA		2.192, 13.613	NA, NA	

^a P-value from Wilcoxon rank-sum test.^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-2
Statistical Comparison Between Smokers and Non-Smokers by Gender of 24-Hour Urine Biomarkers of Exposure by Timepoint and Overall
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Biomarker: Trans-3-hydroxycotinine-O-glucuronide ((nmol/mg Creatinine)/cigarette per day)				Analytical Lab: INBIFO			
Timepoint	Statistic	Smokers	Male Non-Smokers	P-value ^a	Smokers	Female Non-Smokers	P-value ^a
Week 1	N	3		NA	3		NA
	MEAN, GEO MEAN	0.188, 0.186			0.341, 0.257		
	SD, SE	0.0310, 0.0179			0.3146, 0.1816		
	MEDIAN	0.199			0.203		
	MIN, MAX	0.153, 0.212			0.119, 0.701		
	5%, 95%	0.153, 0.212			0.119, 0.701		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	3		NA	3		NA
	MEAN, GEO MEAN	0.380, 0.364			0.377, 0.310		
	SD, SE	0.1248, 0.0721			0.2266, 0.1308		
	MEDIAN	0.415			0.487		
	MIN, MAX	0.241, 0.483			0.116, 0.527		
	5%, 95%	0.241, 0.483			0.116, 0.527		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	2		NA	3		NA
	MEAN, GEO MEAN	0.224, 0.193			0.424, 0.227		
	SD, SE	0.1591, 0.1125			0.3900, 0.2252		
	MEDIAN	0.224			0.425		
	MIN, MAX	0.111, 0.336			0.034, 0.814		
	5%, 95%	0.111, 0.336			0.034, 0.814		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	3		NA	3		NA
	MEAN, GEO MEAN	0.261, 0.256			0.381, 0.302		
	SD, SE	0.0604, 0.0349			0.2833, 0.1636		
	MEDIAN	0.269			0.344		
	MIN, MAX	0.197, 0.317			0.118, 0.681		
	5%, 95%	0.197, 0.317			0.118, 0.681		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhalate Biomarkers of Exposure by Timepoint and Overall
(Page 1 of 8)

Biomarker: Acetonitrile (nL/L @20 °C and 1 atm)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	0.7901	32	35	0.0002
	MEAN, GEO MEAN	15754.045, 7332.378	16887.867, 6839.605		11093.484, 1657.422	28284.236, 12848.032	
	SD, SE	17664.0308, 4163.4520	15733.5078, 2872.5324		15308.4181, 2706.1716	23013.5378, 3889.9979	
	MEDIAN	8240.636	11778.782		439.902	26967.495	
	MIN, MAX	278.352, 61266.718	27.047, 49048.904		27.047, 59118.236	67.737, 90418.051	
	5%, 95%	278.352, 61266.718	27.047, 48597.939		27.047, 43336.359	117.403, 74719.187	
	# of BLQ/ALQ Values	0/0	2/0		3/12	0/0	
Week 3	N	17	30	0.6821	29	35	<.0001
	MEAN, GEO MEAN	22880.217, 14798.644	21214.534, 11055.740		9968.381, 1982.888	29221.367, 22721.461	
	SD, SE	15007.5911, 3639.8755	14479.2885, 2643.5443		13594.3382, 2524.4052	15275.1163, 2581.9659	
	MEDIAN	20360.146	21017.801		360.626	29414.335	
	MIN, MAX	149.199, 55212.198	27.047, 48358.890		27.047, 49646.042	703.834, 64440.436	
	5%, 95%	149.199, 55212.198	189.826, 43703.135		360.626, 32770.330	2753.207, 61151.620	
	# of BLQ/ALQ Values	0/0	1/0		1/14	0/0	
Week 6	N	14	30	0.4727	28	35	<.0001
	MEAN, GEO MEAN	20748.758, 12721.143	24034.251, 14231.801		9852.411, 1891.929	27014.430, 21519.138	
	SD, SE	17703.5189, 4731.4644	15534.1998, 2836.1439		12788.1351, 2416.7304	12362.5750, 2089.6566	
	MEDIAN	18654.588	26642.053		902.786	29207.255	
	MIN, MAX	1827.506, 57117.622	143.554, 49916.584		27.047, 38261.231	285.948, 58955.534	
	5%, 95%	1827.506, 57117.622	178.106, 47862.018		27.047, 37095.541	3549.774, 42384.015	
	# of BLQ/ALQ Values	0/0	0/0		2/12	0/0	
Overall*	N	18	30	0.6471	32	35	<.0001
	MEAN, GEO MEAN	20916.196, 16007.373	20712.218, 17837.694		10449.102, 2925.608	28173.345, 25135.704	
	SD, SE	14849.8295, 3500.1384	10044.1152, 1833.7962		11449.4562, 2023.9970	11605.9501, 1961.7636	
	MEDIAN	20159.243	20099.064		10269.940	25457.817	
	MIN, MAX	2442.621, 61266.718	4509.427, 36405.750		138.408, 41598.061	2561.353, 52452.649	
	5%, 95%	2442.621, 61266.718	5069.379, 35262.657		249.433, 37974.737	10434.097, 51706.482	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 2 of 8)

Biomarker: Acetonitrile (nmol/L)		Analytical Lab: Madison					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value*	Smokers	Non-Smokers	P-value*
Week 1	N	18	30	0.7901	32	35	0.0002
	MEAN, GEO MEAN	654.891, 304.805	702.023, 284.315		461.152, 68.896	1175.766, 534.088	
	SD, SE	734.2880, 173.0733	654.0369, 119.4102		636.3660, 112.4947	956.6653, 161.7059	
	MEDIAN	342.561	489.640		18.287	1121.030	
	MIN, MAX	11.571, 2546.837	1.124, 2038.947		1.124, 2457.526	2.816, 3758.649	
	5%, 95%	11.571, 2546.837	1.124, 2020.200		1.124, 1801.478	4.880, 3106.052	
	# of BLQ/ALQ Values	0/0	2/0		3/12	0/0	
Week 3	N	17	30	0.6821	29	35	<.0001
	MEAN, GEO MEAN	951.123, 615.174	881.881, 459.579		414.382, 82.427	1214.723, 944.523	
	SD, SE	623.8607, 151.3084	601.8992, 109.8913		565.1123, 104.9387	634.9816, 107.3315	
	MEDIAN	846.365	873.703		14.991	1222.744	
	MIN, MAX	6.202, 2295.153	1.124, 2010.263		1.124, 2063.770	29.258, 2678.768	
	5%, 95%	6.202, 2295.153	7.891, 1816.725		14.991, 1362.252	114.450, 2542.053	
	# of BLQ/ALQ Values	0/0	1/0		1/14	0/0	
Week 6	N	14	30	0.4727	28	35	<.0001
	MEAN, GEO MEAN	862.519, 528.814	999.096, 591.613		409.561, 78.645	1122.981, 894.544	
	SD, SE	735.9294, 196.6854	645.7516, 117.8976		531.5986, 100.4627	513.9081, 86.8663	
	MEDIAN	775.466	1107.502		37.529	1214.136	
	MIN, MAX	75.969, 2374.361	5.968, 2075.016		1.124, 1590.507	11.887, 2450.762	
	5%, 95%	75.969, 2374.361	7.404, 1989.608		1.124, 1542.049	147.563, 1761.890	
	# of BLQ/ALQ Values	0/0	0/0		2/12	0/0	
Overall*	N	18	30	0.6471	32	35	<.0001
	MEAN, GEO MEAN	869.479, 665.421	861.000, 741.507		434.366, 121.616	1171.157, 1044.883	
	SD, SE	617.3025, 145.4996	417.5306, 76.2303		475.9501, 84.1369	482.4556, 81.5499	
	MEDIAN	838.013	835.512		426.918	1058.273	
	MIN, MAX	101.539, 2546.837	187.455, 1513.375		5.753, 1729.218	106.475, 2180.439	
	5%, 95%	101.539, 2546.837	210.732, 1465.857		10.369, 1578.597	433.742, 2149.422	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 3 of 8)

Biomarker: Acetonitrile (nL/L @20 °C and 1 atm)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	953.850, 577.813			1160.703, 125.504		
	SD, SE	746.7132, 176.0020			3324.8895, 587.7630		
	MEDIAN	719.529			90.156		
	MIN, MAX	25.305, 2663.770			1.378, 18842.877		
	5%, 95%	25.305, 2663.770			1.591, 2955.912		
	# of BLQ/ALQ Values	0/0			3/12		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2622.262, 1391.928			732.205, 143.450		
	SD, SE	3152.9384, 764.6999			1258.1956, 233.6411		
	MEDIAN	1710.761			90.156		
	MIN, MAX	24.866, 13126.227			1.803, 6205.755		
	5%, 95%	24.866, 13126.227			17.173, 2148.910		
	# of BLQ/ALQ Values	0/0			1/14		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	2866.473, 991.480			810.226, 138.864		
	SD, SE	5255.7683, 1404.6632			1311.2932, 247.8111		
	MEDIAN	882.790			122.771		
	MIN, MAX	121.834, 19039.207			1.352, 5729.977		
	5%, 95%	121.834, 19039.207			9.016, 3091.295		
	# of BLQ/ALQ Values	0/0			2/12		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2093.350, 1373.434			940.679, 228.053		
	SD, SE	2476.1737, 583.6397			1403.8877, 248.1746		
	MEDIAN	1321.457			568.547		
	MIN, MAX	152.371, 11017.118			6.920, 7000.268		
	5%, 95%	152.371, 11017.118			14.672, 3072.898		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., '<1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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Protocol No. PM-8450

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Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 4 of 8)

Biomarker: Acetonitrile ((nmol/L)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	39.651, 24.019			48.250, 5.217		
	SD, SE	31.0407, 7.3164			138.2145, 24.4331		
	MEDIAN	29.911			3.748		
	MIN, MAX	1.052, 110.732			0.057, 783.292		
	5%, 95%	1.052, 110.732			0.066, 122.876		
	# of BLQ/ALQ Values	0/0			3/12		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	109.007, 57.863			30.438, 5.964		
	SD, SE	131.0667, 31.7883			52.3027, 9.7124		
	MEDIAN	71.116			3.748		
	MIN, MAX	1.034, 545.653			0.075, 257.971		
	5%, 95%	1.034, 545.653			0.714, 89.329		
	# of BLQ/ALQ Values	0/0			1/14		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	119.158, 41.216			33.681, 5.772		
	SD, SE	218.4806, 58.3914			54.5100, 10.3014		
	MEDIAN	36.698			5.104		
	MIN, MAX	5.065, 791.454			0.056, 238.193		
	5%, 95%	5.065, 791.454			0.375, 128.504		
	# of BLQ/ALQ Values	0/0			2/12		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	87.020, 57.093			39.104, 9.481		
	SD, SE	102.9338, 24.2617			58.3592, 10.3165		
	MEDIAN	54.933			23.634		
	MIN, MAX	6.334, 457.978			0.288, 290.999		
	5%, 95%	6.334, 457.978			0.610, 127.739		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

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Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 5 of 8)

Biomarker: Acetonitrile (ng/mL)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value*	Female		P-value*
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18	30	0.7901	32	35	0.0002
	MEAN, GEO MEAN	4368528.81, 2033236.87	4682932.74, 1896592.77		3076175.19, 459595.94	7843096.71, 3562703.96	
	SD, SE	4898159.534, 1154507.274	4362833.819, 796540.832		4244958.260, 750409.693	6381554.714, 1078679.624	
	MEDIAN	2285092.74	3266205.46		121982.93	7477970.11	
	MIN, MAX	77185.89, 16988996.62	7500.00, 13601049.39		7500.00, 16393231.66	18783.13, 25072535.47	
	5%, 95%	77185.89, 16988996.62	7500.00, 13475998.91		7500.00, 12016985.39	32555.43, 20719308.03	
	# of BLQ/ALQ Values	0/0	2/0		3/12	0/0	
Week 3	N	17	30	0.6821	29	35	<.0001
	MEAN, GEO MEAN	6344585.35, 4103599.50	5882698.71, 3065708.47		2764189.11, 549846.06	8107959.01, 6300562.94	
	SD, SE	4161540.283, 1009321.774	4015044.251, 733043.435		3769651.314, 700006.675	4235723.858, 715968.008	
	MEDIAN	5645780.58	5828145.56		100000.00	8156468.27	
	MIN, MAX	41372.11, 15310104.26	7500.00, 13409711.46		7500.00, 13766633.29	195170.00, 17869054.85	
	5%, 95%	41372.11, 15310104.26	52637.82, 12118690.88		100000.00, 9087071.06	763452.42, 16957080.35	
	# of BLQ/ALQ Values	0/0	1/0		1/14	0/0	
Week 6	N	14	30	0.4727	28	35	<.0001
	MEAN, GEO MEAN	5753540.94, 3527517.98	6664594.20, 3946417.12		2732031.12, 524623.46	7490984.97, 5967164.07	
	SD, SE	4909109.398, 1312014.674	4307566.587, 786450.463		3546094.683, 670148.904	3428088.702, 579452.750	
	MEDIAN	5172836.64	7387726.31		250338.69	8099045.75	
	MIN, MAX	506759.43, 15838470.03	39806.96, 13841653.46		7500.00, 10609674.23	79292.12, 16348115.24	
	5%, 95%	506759.43, 15838470.03	49387.99, 13271931.02		7500.00, 10286433.44	984337.01, 11752904.36	
	# of BLQ/ALQ Values	0/0	0/0		2/12	0/0	
Overall*	N	18	30	0.6471	32	35	<.0001
	MEAN, GEO MEAN	5799970.77, 4438775.34	5743408.55, 4946315.64		2897490.82, 811258.37	7812346.90, 6970022.10	
	SD, SE	4117793.672, 970573.276	2785189.825, 508503.765		3174884.807, 561245.644	3218279.899, 543988.590	
	MEDIAN	5590070.97	5573383.75		2847810.05	7039342.90	
	MIN, MAX	677328.28, 16988996.62	1250444.51, 10095157.32		38379.95, 11534962.73	710251.93, 14544893.17	
	5%, 95%	677328.28, 16988996.62	1405716.91, 9778182.78		69166.67, 10530230.80	2893329.99, 14337984.28	

* P-value from Wilcoxon rank-sum test.

* Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics).

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Covance CRU Study No. 12226-8450

Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 6 of 8)

Biomarker: Acetonitrile ((ng/mL)/cigarette per day)		Analytical Lab: Madison					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	264498.41, 160224.97			321857.83, 34801.41		
	SD, SE	207060.351, 48804.593			921977.527, 162984.140		
	MEDIAN	199522.37			25000.00		
	MIN, MAX	7016.90, 738652.03			381.99, 5225048.61		
	5%, 95%	7016.90, 738652.03			441.18, 819661.58		
	# of BLQ/ALQ Values	0/0			3/12		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	727142.10, 385975.96			203037.18, 39778.17		
	SD, SE	874296.238, 212047.985			348892.197, 64787.654		
	MEDIAN	474386.68			25000.00		
	MIN, MAX	6895.35, 3639846.15			500.00, 1720829.16		
	5%, 95%	6895.35, 3639846.15			4761.90, 595883.42		
	# of BLQ/ALQ Values	0/0			1/14		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	794860.55, 274933.00			224672.24, 38506.79		
	SD, SE	1457401.900, 389507.042			363615.941, 68716.954		
	MEDIAN	244793.85			34043.74		
	MIN, MAX	33783.96, 5279490.01			375.00, 1588897.93		
	5%, 95%	33783.96, 5279490.01			2500.00, 857202.79		
	# of BLQ/ALQ Values	0/0			2/12		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	580476.83, 380847.28			260846.18, 63238.54		
	SD, SE	686632.314, 161840.789			389291.964, 68817.747		
	MEDIAN	366434.34			157655.55		
	MIN, MAX	42251.86, 3054999.42			1919.00, 1941144.01		
	5%, 95%	42251.86, 3054999.42			4068.63, 852101.27		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234' for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

Protocol No. PM-8450

Covance CRU Study No. 12226-8450

Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhalate Biomarkers of Exposure by Timepoint and Overall
(Page 7 of 8)

Biomarker: Carbon monoxide (ppm)		Analytical Lab: CRF					
Timepoint	Statistic	Male			Female		
		Smokers	Non-Smokers	P-value ^a	Smokers	Non-Smokers	P-value ^a
Week 1	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	25.9, 22.4	5.9, 5.8		26.5, 22.6	5.5, 5.3	
	SD, SE	15.45, 3.64	1.34, 0.24		14.82, 2.62	1.35, 0.23	
	MEDIAN	23.5	6.0		25.0	5.2	
	MIN, MAX	8.6, 71.4	3.6, 9.1		7.8, 66.5	3.7, 9.6	
	5%, 95%	8.6, 71.4	3.7, 8.0		8.4, 54.7	4.0, 8.1	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 2	N	18	30	<.0001	31	35	<.0001
	MEAN, GEO MEAN	23.0, 19.6	5.9, 5.2		25.3, 20.7	4.5, 4.3	
	SD, SE	11.96, 2.82	1.64, 0.30		17.42, 3.13	1.27, 0.22	
	MEDIAN	21.5	5.9		21.2	4.3	
	MIN, MAX	4.5, 44.1	0.1, 9.6		6.5, 88.9	2.1, 8.6	
	5%, 95%	4.5, 44.1	4.0, 8.5		6.7, 55.6	2.2, 6.8	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 3	N	17	30	<.0001	29	35	<.0001
	MEAN, GEO MEAN	26.3, 21.5	6.1, 6.0		26.3, 22.8	4.5, 4.2	
	SD, SE	16.80, 4.07	1.56, 0.28		13.29, 2.47	1.33, 0.23	
	MEDIAN	23.1	6.0		24.7	4.4	
	MIN, MAX	5.3, 62.2	3.4, 10.6		5.3, 60.7	0.3, 7.4	
	5%, 95%	5.3, 62.2	4.0, 9.4		7.2, 45.1	3.0, 6.9	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Week 6	N	14	30	<.0001	28	35	<.0001
	MEAN, GEO MEAN	28.8, 23.6	7.4, 7.0		29.4, 25.8	5.2, 4.6	
	SD, SE	17.34, 4.63	2.44, 0.45		13.38, 2.53	1.99, 0.34	
	MEDIAN	25.6	6.9		27.9	5.0	
	MIN, MAX	5.0, 70.5	4.5, 13.8		4.0, 54.0	0.4, 9.8	
	5%, 95%	5.0, 70.5	4.8, 13.3		10.1, 51.1	1.0, 9.0	
	# of BLQ/ALQ Values	0/0	0/0		0/0	0/0	
Overall ^b	N	18	30	<.0001	32	35	<.0001
	MEAN, GEO MEAN	25.3, 21.7	6.3, 6.2		26.6, 22.9	4.9, 4.9	
	SD, SE	14.20, 3.35	1.09, 0.20		14.37, 2.54	0.81, 0.14	
	MEDIAN	23.0	6.3		22.0	5.0	
	MIN, MAX	5.9, 60.3	4.4, 8.6		8.2, 66.0	3.1, 6.6	
	5%, 95%	5.9, 60.3	5.0, 8.0		9.5, 49.2	3.4, 6.3	

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.

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RSR

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Table 14.2.2-3
Statistical Comparison Between Smokers and Non-Smokers by Gender of Exhale Biomarkers of Exposure by Timepoint and Overall
(Page 8 of 8)

Biomarker: Carbon monoxide ((ppm)/cigarette per day)		Analytical Lab: CRF					
Timepoint	Statistic	Male		P-value ^a	Female		P-value ^a
		Smokers	Non-Smokers		Smokers	Non-Smokers	
Week 1	N	18		NA	32		NA
	MEAN, GEO MEAN	2.5, 1.8			2.1, 1.7		
	SD, SE	3.09, 0.73			1.67, 0.29		
	MEDIAN	1.6			1.6		
	MIN, MAX	0.6, 14.3			0.5, 9.1		
	5%, 95%	0.6, 14.3			0.7, 5.0		
	# of BLQ/ALQ Values	0/0			0/0		
Week 2	N	18		NA	31		NA
	MEAN, GEO MEAN	2.6, 1.6			2.1, 1.7		
	SD, SE	4.90, 1.16			1.50, 0.27		
	MEDIAN	1.5			1.6		
	MIN, MAX	0.5, 22.1			0.5, 8.1		
	5%, 95%	0.5, 22.1			0.8, 4.9		
	# of BLQ/ALQ Values	0/0			0/0		
Week 3	N	17		NA	29		NA
	MEAN, GEO MEAN	2.6, 2.0			1.8, 1.7		
	SD, SE	2.39, 0.58			0.99, 0.18		
	MEDIAN	1.9			1.6		
	MIN, MAX	0.6, 11.0			0.8, 5.5		
	5%, 95%	0.6, 11.0			0.8, 3.8		
	# of BLQ/ALQ Values	0/0			0/0		
Week 6	N	14		NA	28		NA
	MEAN, GEO MEAN	4.0, 1.9			2.2, 1.9		
	SD, SE	9.03, 2.41			1.60, 0.30		
	MEDIAN	1.7			1.8		
	MIN, MAX	0.6, 35.3			0.7, 7.3		
	5%, 95%	0.6, 35.3			1.1, 6.8		
	# of BLQ/ALQ Values	0/0			0/0		
Overall ^b	N	18		NA	32		NA
	MEAN, GEO MEAN	2.8, 1.8			2.1, 1.8		
	SD, SE	4.52, 1.07			1.14, 0.20		
	MEDIAN	1.8			1.8		
	MIN, MAX	0.6, 20.7			0.8, 5.3		
	5%, 95%	0.6, 20.7			0.8, 5.1		

NOTE: Values listed were normalized by taking the original biomarker and dividing it by the number of cigarettes found in question 4 of the weekly survey for the corresponding week.

^a P-value from Wilcoxon rank-sum test.

^b Overall values calculated by first averaging the results across visits within a subject, then calculating the descriptive statistics across subjects. Count of BLQ/ALQ values does not apply as the BLQ/ALQ values were converted to the limit of the quantification (e.g., <1.234' will be used as '1.234') for the averages across visits within a subject thus eliminating all BLQ/ALQ values for the overall statistics.